Expanding Coverage of Oncology Drugs in an Aging, Upper-Middle-Income Country: Analyses of Public and Private Expenditures in Chile

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Abstract

Purpose The population of Chile has aged, and in 2017, cancer became the leading cause of death. Since 2005, a national health program has expanded coverage of drugs for 13 types of cancer and related palliative care. We describe the trends in public and private oncology drug expenditures in Chile and consider how increasing expenditures might be addressed.

Methods We analyzed total quarterly drug expenditures for 131 oncology drugs from quarter (Q)3 2012 until Q1 2017, including public and private insurance payments and patient out-of-pocket spending. The data were analyzed by drug-mix, sources of funding, growth, and intellectual property status. The Laspeyres Price Index was used to analyze expenditure growth.

Results We found 131 oncology drugs associated with 87,129 observations. Spending on drugs rose 120% from the first period, spanning from the first 3 quarters (Q3, Q4, Q1 2012-2013) to the last period (Q3, Q4, Q1 2016-2017), corresponding to an annualized rate of 19.2% and totaling US$398 million (in 2017 dollars). The public sector accounted for 84.2% of spending, which included 50 drugs in the official treatment protocols, whereas private insurance accounted for 7.3% in on-protocol drugs. The remaining 8.5% was paid out of pocket. In the public sector, more than 90% of growth resulted from increased use. Seven drugs, including 3 with nonexpired patents, accounted for 50% of total expenditures.

Conclusion Increased use and access enabled by expanded public expenditures drove most of the growth in oncology drug expenditures. However, the rate of public expenditure growth may be fiscally unsustainable. Policies are urgently needed to promote the use of generic drugs, the appropriate mix of on-protocol versus off-protocol drugs, and the curbing of off-label prescribing.

Introduction

As life expectancy in Chile has reached 77 years for men and 83 years for women, cancer prevalence and mortality have increased. The cancer mortality rate was estimated to be approximately 156 per 100,000 in 2018, approaching the higher rates of 164 in upper-middle-income countries and 230 in high-income countries. For more than 2 decades, cancer was the second leading cause of death after cardiovascular disease, but overtook cardiovascular disease in 2017, growing at a rate of 31.2 per 100,000 from 1997 to 2017, faster than upper-income and upper-middle-income countries. The highest rates of cancer mortality for men are for stomach (26.0 per 100,000), prostate (25.2 per 100,000), and lung (22.8 per 100,000) cancer, and among women, breast (18.4 per 100,000), colorectal (17.3 per 100,000), and stomach (12.4 per 100,000) cancer. Cancer mortality in the age group under 15 years is estimated at 3.3 per 100,000, led by leukemia (1.6 per 100,000).

In 2014, pharmaceutical expenditures in Chile totaled US$3.9 billion, which represented approximately 1.5% of gross domestic product, or 19.2% of total health expenditures. This proportion was above the Organisation for Economic Co-Operation and Development countries’ average of 1.4% and 15.9%, respectively. Public and private insurance covered approximately 40%-60% of total pharmaceutical expenditures. The remaining drugs were sold in private pharmacies and paid out of pocket (OOP). In 2015, 32.2% of total health expenditures were paid OOP, and 30%-32% of total OOP spending was devoted to pharmaceuticals. Public and private spending on cancer drugs in Chile has not been studied.

The Health System and Oncology Drugs

Approximately 75% of the population is covered by the Fondo Nacional de Salud (FONASA), 18% by private health insurance (Instituciones de Salud...
Previsional (ISAPREs), 3% by the Ministry of Defense, and the remaining by other programs.\textsuperscript{11}

In 2005, a mandatory program, AUGE (Universal Access with Explicit Guarantees), was initiated to address non-communicable diseases and injuries.\textsuperscript{12} Since then, AUGE has expanded and as of 2018, covers 80 health conditions and interventions, including 13 types of cancer and associated palliative care (Table 1). There are guiding protocols for each cancer type, including a list of recommended drugs that should be available in public and private facilities (Appendix Table A1).\textsuperscript{13} In 2016, a public fund (Ricate Soto) was created to subsidize high-cost pharmaceuticals, including trastuzumab, a treatment of breast cancer.\textsuperscript{14} Under both programs, drugs are provided free of charge in the public system, whereas patients with private insurance pay a 20% copayment.

**Regulatory Framework**

Drugs used for cancer treatment can be categorized into originator branded and generics (including branded generics). Unbranded generics are marketed using the name of the active ingredient, whereas branded generics use a name other than the active ingredient. Originator-branded drugs are often protected by either patents or data exclusivities. Patents allow their holders to exclude others from manufacturing or selling the product covered by the patent for 20 years from the date of patent filing, whereas data exclusivity provides rights to originator companies for 5 years after new drug approval.\textsuperscript{15} In Chile, the prices of originator-branded drugs are among the highest in Latin America, whereas the prices of generics are among the lowest.\textsuperscript{16} The price difference between unbranded generics and originator-branded drugs is approximately 10- to 15-fold.\textsuperscript{16,17}

Measured by volume, generics account for 47% of the Chilean market, but if branded generics are included, this figure increases to 88%.\textsuperscript{16} One important cost-containment policy is to promote generic substitution after the patents on originator-branded medicines expire.\textsuperscript{18} In 2008, a bioequivalence program was launched that required generic manufacturers to demonstrate equivalence with the original drug. The program has been gradually implemented.\textsuperscript{19,20}

**Objectives**

We analyzed trends in public and private spending on oncology drugs in Chile from 2012-2017. To our knowledge, this article is the first to aggregate such expenditures.

Specifically, we aimed to:

- Estimate the size, mix, and growth of oncology drug expenditures;
- Identify the main sources of funding for oncology drugs;
- Analyze factors that contributed to the growth of oncologic drug expenditures, namely price, use, and the introduction of new drugs;

**CONTEXT**

**Key Objective**
To examine spending on oncology drugs in Chile, a transitioning upper-middle-income country in which cancer recently became the leading cause of death.

**Knowledge Generated**
From 2012-2017, expenditures on oncology drugs increased by an annualized rate of 19.2%, 3 times faster than total health expenditures (6.3%). Seven drugs accounted for half of the total expenditures. Growth was primarily driven by expenditures on originator-branded drugs.

**Relevance**
Policies are urgently needed to address the appropriate mix of generic and branded products, including a pathway for accelerating biosimilar approval, and purchasing models based on value.

### TABLE 1. Cancers Included in the National Programs, 2005-2018

| Year Added | Type                                |
|------------|-------------------------------------|
| 2005       | Cervical cancer                     |
|            | Breast cancer                       |
|            | Testicular cancer                   |
|            | Lymphoma                            |
|            | Pediatric cancer (< 15 years of age) |
|            | Pain relief and palliative care     |
| 2006       | Gastric cancer                      |
|            | Prostate cancer                     |
| 2007       | Leukemia                            |
|            | Brain and other tumors of the CNS   |
| 2013       | Colorectal cancer                   |
|            | Ovarian cancer                      |
|            | Bladder cancer                      |
|            | Osteosarcoma                        |
| 2016       | High-cost fund: trastuzumab for breast cancer |

**NOTE.** Diseases covered by Universal Access With Explicit Guarantees (AUGE) and date of incorporation.\textsuperscript{44}
• Discuss the impact of policies of the Ministry of Health by estimating the share of drug expenditures corresponding to medicines listed versus not listed in the treatment protocols.

**METHODOLOGY**

**Data Sources**

We obtained data from the only robust sources available: public sector pharmaceutical data gathered by the national procurement agency Central Nacional de Abastecimiento (CENABAST).\(^{21,22}\) and private pharmacies sales data aggregated by IQVIA-Chile.\(^{23,24}\)

The CENABAST database includes procurement information from all public sector entities, including CENABAST; pharmacies; hospitals, including those of the Armed Forces and universities; health centers; regional health services; and municipalities. We extracted volume and expenditure information from 86,827 transactions of 121 oncology drugs. The database includes the transaction number, date of purchase, active substance name, dosage form, route of administration, number of units, unit price, buying institution, supplier or drug company name, and drug class, as defined by the Anatomic Classification of Pharmaceutical Products of the European Pharmaceutical Market Research Association (EphMRA).\(^{25}\) Data on generic versus brand status were not available in the CENABAST dataset for all transactions. When not available, company Web sites and information from the IQVIA dataset were consulted (Appendix Table A2). We also triangulated with the registry of market authorizations of the Institute of Public Health.\(^{26}\)

The private sales dataset from IQVIA consisted of 302 observations associated with 113 drugs that were sold in private pharmacies from July 2012 to March 2017. The dataset included the following information: chemical and commercial name of the molecule; classification as originator branded, unbranded generic, or branded generic; dosage and number of units; sales revenues; route of administration; manufacturer name; drug class; and prescription versus over-the-counter status. The dataset does not include information on private hospitals and clinics.

Small-molecule or biologic status was determined from the DrugBank,\(^{27}\) and approval dates were sourced from the CenterWatch Web site (Appendix Table A3).\(^{28}\) We developed a protocol to assess patent status in Chile based on the US Food and Drug Administration’s Orange Book\(^{29}\) and then consulted the Chilean National Institute of Industrial Property (INAPI) Web site.\(^{30}\) Information regarding data exclusivity and availability of biosimilars was obtained from the Chilean Institute of Public Health Web site.\(^{31,32}\)

**Outcome Variables**

Out of each dataset, the following variables were generated:

1. Oncology drug variable, using class L antineoplastic and immunomodulating agents from EphMRA, excluding nonspecific cancer drugs, as, for example, those for preventing organ rejection.

2. Categorical variables for oncology drugs: (i) small molecule or biologic, (ii) included or excluded from the Ministry of Health protocols, (iii) with/without patent(s), (iv) with/without biosimilars, and (v) with/without data exclusivity protection.

3. Sources of spending: (i) public sector, including CENABAST; hospitals, including the Armed Forces and universities, health centers, regional health services, and municipalities; and (ii) private sector, including private insurance and OOP spending. Because private insurance reimburses prescribed on-protocol drugs sold at retail pharmacies, and off-protocol coverage is not specified, we assumed that all on-protocol drugs sold in private retail pharmacies were covered by private insurance and that all off-protocol drugs were paid OOP.

4. Total drug expenditures by quarter from Q3 2012 until Q1 2017 calculated by adding the value in Chilean pesos (CLP of all prescribed drugs) spent in the public and private sectors. All expenditures were adjusted to CLP of Q1 2017 and then converted to constant 2017 US$ using the 2017 first-quarter average exchange rate, as reported by the Chilean Central Bank.\(^{33}\)

5. Total drug expenditures in constant 2017 US$ by individual drugs.

6. Relative contribution to growth was estimated by comparing expenditures during 2 periods: an initial period spanning Q3, Q4, and Q1 of 2012-2013 and the last period spanning Q3, Q4, and Q1 of 2016-2017. Expenditure changes of (i) price; (ii) volume (total number of standardized doses by molecule in the public dataset and defined daily doses per 100 in the private dataset); and (iii) new drugs, defined as those with sales only during the last period. An index for on- and off-protocol drugs was estimated for the public and private sector in 2 steps: (i) the Laspeyres Price Index measuring the change in prices of the initial group of drugs relative to the base period and a volume effect equal to the difference in expenditures between periods minus the price effect, plus (ii) total spending on new drugs.

We used STATA (version 15; STATA, College Station, TX) to perform statistical analysis.

**RESULTS**

From July 2012 through March 2017, a period of 19 quarters, expenditures on cancer drugs in the public and private sectors reached $398 million (in 2017 US dollars) and included 131 drugs (Fig 1). Of this, $335 million (84.2%) was spent by the public sector, including $234 million (70.0%) for on-protocol drugs to treat 13 cancer types and related palliative care. Sales of on-protocol drugs at retail pharmacies reached $29 million (7.5%), whereas $34 million (8.3%) was spent OOP on off-protocol medicines.
Expenditures Over Time

From the first 3 quarters (Q3, Q4, Q1 2012-2013) to the last three (Q3, Q4, Q1 2016-2017), total expenditures on cancer drugs increased by 120% (annualized rate of 19.2%). Public spending on the 50 on-protocol drugs to treat the 13 priority cancers and palliative care increased 127%, or an annualized rate of 20.0%. Public spending on off-protocol drugs increased by 156%, equivalent to an annualized rate of 23.3%. Public expenditures displayed seasonal variations associated with public procurement practices according to the annual budget cycle. By contrast, expenditures paid by private insurance for on-protocol drugs expanded gradually, increasing 38% over the study period, or 7.4% per year, whereas those paid OOP rose 72%, or 12.9% annually.

Factors Contributing to Growth in Expenditures

We controlled for any seasonality comparing the same quarters from the initial period (Q3, Q4, Q1 of 2012-2013) versus the final period (Q3, Q4, Q1 of 2016-2017). There was a significant difference in the growth rate by sectors and contributing factors ($\chi^2 = 197.88; df = 6; P < .0001$). More than 90% of the growth in public sector expenditures was driven by an increase in use, with the remaining attributable to price increases. Similarly, in the public off-protocol group, use accounted for most expenditure growth. Approximately 58% of private insurance expenditure growth for on-protocol cancer drugs was associated with price increases. Finally, 45% of the growth of OOP expenditures was driven by use of new medicines (Fig 2).

Small-Molecule Drugs and Biologics

Of 131 drugs, 108 (82%) were small-molecule drugs, and 23 (18%) were biologics, corresponding to expenditures of US$266 million (66.8%) and US$132 million (33.2%), respectively. Overall, 24 drugs (18.3%) had a corresponding approved generic product, all of which were small-molecule drugs. Twenty drugs (15%) were protected by data exclusivity, including 6 (30%) biologicals.

Expenditures by Brand Versus Generic Products

Originator-branded drugs dominated total spending, accounting for 72% (Fig 3). Within the originator-branded category, public payers accounted for 84% of expenditures. Similarly, public payers accounted for 83% of total sales of generics and branded generics. There was a significant difference in expenditures by sectors and drug products—originator branded, branded generic, and unbranded generic ($\chi^2 = 70.68; df = 6; P < .0001$). For example, the share of expenditures on originator-branded on-protocol drugs in the public sector reached 80.8% versus 65.5% in private insurance plans. For off-protocol drugs, the percentage of originator-branded drugs was 55.6% in the public sector and 77.4% for medications purchased OOP.

Top 7 Drugs

Public and private spending on cancer medicines was heavily concentrated, with 7 drugs accounting for 50% of total public and private expenditures. Of 131 oncologic drugs, the top 7 drugs were trastuzumab, rituximab, dasatinib, imatinib, triptorelin, nilotinib, and methotrexate (Fig 4). These drugs were used for the treatment of leukemia, non-Hodgkin lymphoma, bone, prostate, and breast cancers. Of the top 7, all except triptorelin (a prostate cancer treatment) were part of the official protocols. Of the top 7, 2 were biologics, and 3 had patents in Chile: trastuzumab (patent issued: 2018); imatinib (patent issued: 2014); and nilotinib (patent issued: 2008). None of the 7 had data exclusivity.
Factors contributing to growth of oncologic drug expenditures: comparison between Quarter (Q)3, 4, 1, 2012-2013 versus Q 3, 4, 1, 2016-2017 (in percent). OOP, out of pocket.

**DISCUSSION**

Because cancer became the leading cause of death around 2017, our data show that the government allocated significant resources to oncology drugs. During the study period, total expenditures on such drugs increased by 120%, or an annualized rate of 19.2%, 3 times the growth rate of total health expenditures (6.33% per year). Growth in public sector spending on oncology drugs was slightly higher, at 136%, or 21% annualized, more than 3 times the growth rate of the public health budget (6.53% per year). Annual growth in public spending on oncology drugs in Chile was much higher than worldwide annual spending growth on oncology drugs (21.0% v 11.8%).

Drug expenditure per capita was US$439 in the worldwide reference group, compared with US$439 in the worldwide reference group. Although Chile is transitioning to a high-income economy, a continuous trend of increased spending on cancer drugs may be fiscally unsustainable.

Increased volume associated with expanded coverage rather than price increases was the driving force underlying increased spending in the public sector, accounting for approximately 94% of such growth. In contrast, increasing prices accounted for 58% of expenditure growth in on-protocol drugs for private insurers. These results suggest that the public sector has been more successful in containing price increases than the private insurance sector, especially for on-protocol drugs.

One possible explanation for this difference is market power. Although Chile has no drug price control policy, the government is a large buyer and uses the well-established e-platform, ChileCompra, to attract many bidders for off-patent drugs and thereby obtain better prices. In contrast, the private insurance sector consists of smaller players reimbursing prescriptions provided through pharmacies, decreasing their bargaining leverage.

In general, the health system has little means to ensure that the 50 on-protocol drugs are used only for the patient subgroups or the disease stage indicated in the protocols for whom these drugs are likely to be most effective. For example, methotrexate is indicated for acute leukemia but is also used for osteosarcoma, breast cancer, and Hodgkin lymphoma, where benefits are more uncertain. Trastuzumab is recommended for a limited number of breast cancer types but can be used more broadly, its status as the highest-expenditure drug (13% of total oncology drug expenditures) could, therefore, be driven by use in patients for which it is less effective.

Approximately 70% of total public expenditures were for on-protocol drugs. Of the top 7 highest-expenditure drugs, accounting for approximately 50% of total spending, 6 were on protocol, addressing cancers that respond well to drug treatment: for example, imatinib for chronic myeloid leukemia, rituximab for non-Hodgkin lymphoma, and trastuzumab for human epidermal growth factor receptor 2–positive breast cancer. Of the top 7 drugs, nilotinib, and imatinib, trastuzumab remained under patent protection in Chile as of 2019. Biosimilar versions of trastuzumab are beginning to become available elsewhere, but not yet in Chile, where the most-used dose (440 mg) was patented in 2018; although other doses are off patent, no generics have yet entered the market.

There is consensus in the literature that promoting the use of effective generic medicines could improve access and reduce cost without adversely affecting patient care. Chilean regulations mandate that generic drugs be bio-equivalent to branded ones. The drugs listed in the official protocols have been available for approximately 30 years, approved on average in 1988, suggesting a choice by policymakers to control public spending by favoring well-established, off-patent small-molecule drugs. Public health facilities and clinicians’ decisions are being influenced accordingly, because 71% of the total volume of on-protocol drugs are generic or branded generics. However, originator-branded drugs accounted for 80.8% of...
FIG 4. Contribution of each drug to total oncologic drug expenditures, 2012, Quarter (Q)3 to 2017, Q1 (2017 US$ millions).

on-protocol cancer drug expenditures. Among the top 7 drugs, originator-branded products accounted for 83.8% of expenditures, due in part to patent protection. However, there is still room for improvement in the public on-protocol sector; excluding drugs under patent and data protection, originator-branded products account for approximately 28% of volume despite the availability of generics or branded generics.

Off-protocol expenditures have been growing faster than on-protocol expenditures in the public sector, at 156% versus 127%, respectively (Fig 2). Although off-protocol drugs represent approximately 9% of the total volume in the public sector, they represent approximately 30% of total public expenditures. The public health system has limited influence over the choice between generic or nongeneric prescribing, and more expensive branded-original drugs can be used, according to clinician preference, suggesting that some clinicians and health managers prefer newer, not widely used, and more expensive originator-branded drugs, the additional therapeutic value of which is uncertain. Similarly, hospitals and other health facilities have procurement autonomy, even for on-protocol drugs.22 If we exclude drugs under patent and data protection, 30% of the volume of off-protocol drugs in the public sector are originator-branded products (Fig 4). Most generics and branded generics continue to lack bioequivalence proof, potentially discouraging generic use (Appendix Table A3).42,43

This study has limitations; data from private hospitals and clinics were not available, and these sources are estimated to account for approximately 20% of total drug expenditures.6 The datasets did not allow differentiation of oncology from nononcology uses of medications that have multiple indications. For example, rituximab could contribute significantly to expenditures for rheumatoid arthritis, but this is unlikely to change its place in the top 7 drugs. Our findings may also be sensitive to study design choices: we excluded certain adjunct palliative medications but included others with alternate uses, such as dexamethasone. We were unable to compare unit drug prices because public and private volume was reported in different units, but we were able to do so in within-sector comparisons.

In conclusion, total oncology drug expenditures were driven by public sector spending, helping to ensure access for 14.1 million Chileans. However, the rate of growth of oncology drugs was more than 3 times public health expenditure growth, indicating that this trend may be fiscally unsustainable. The Ministry of Health protocols are intended to optimize patient care while maintaining fiscal prudence—approximately 70% of total public oncology expenditures were for on-protocol drugs. However, original-branded drugs dominate the top 7 drugs that account for 50% of total expenditures, including 3 patent-protected drugs. Off-protocol use of newer drugs is expanding. Because cancer is now the leading cause of death, serious consideration should be given to the appropriate mix of on- versus off-protocol drugs, generic versus branded drugs, and the curbing of prescriptions; also, in circumstances in which benefit remains uncertain, by exploring models of purchasing based on value.
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REFERENCES
1. Jimenez de la Jara J, Bastias G, Ferreccio C, et al: A snapshot of cancer in Chile: Analytical frameworks for developing a cancer policy. Biol Res 48:10, 2015
2. Herrera Riquelme CA, Kuhn-Barrientos L, Rosso Astorga R, et al: Tendencia de la mortalidad por cáncer en Chile según diferencias por nivel educacional, 2000-2010 [in Spanish]. Rev Panam Salud Publica 37:44-51, 2016
3. Ced C, Herrera C, Rodríguez R, et al: Assessing the economic impact of cancer in Chile: A direct and indirect cost measurement based on 2009 registries [in Spanish]. Medwave 16:e6509-e6509, 2016
4. International Agency for Research on Cancer, World Health Organization: Cancer today. http://gco.iarc.fr/today/home
5. Institute for Health Metrics and Evaluation: GBD compare. Viz Hub. http://vizhub.healthdata.org/gbd-compare
6. Ministry of Health, Ministry of Finance: Diagnóstico del mercado de medicamentos en Chile, año 2015. http://desal.minsal.cl/wp-content/uploads/2018/03/2018.03.28_Diagn%C3%B3stico-Mercado-Medicamentos-en-Chile-final.pdf
7. OECD: Pharmaceutical spending. https://data.oecd.org/healthres/pharmaceutical-spending.htm
8. Correa-Burrows P: Out-of-pocket health care spending by the chronically ill in Chile. Procedia Econ Finance 121:481-494, 2017
9. Villalobos Dintrans P: Out-of-pocket health expenditure differences in Chile: Insurance performance or selection? Health Policy 122:184-191, 2018
10. FONASA: Estadísticas institucionales. http://datos.gob.cl/organization/fondo_nacional_de_salud
11. Vargas V, Poblete S: Health prioritization: The case of Chile. Health Aff (Millwood) 27:782-792, 2008
12. Ministry of Health: Listado de prestaciones específico regímen de garantías explícitas en salud. https://diprece.minsal.cl/wp-content/uploads/2018/03/Lep_incluye-Decreto-8-de-2018.pdf
13. García JL, Vergara-Mardones H, Escobar L, et al: The medicines situation in Chile: A critical appraisal from the academy. Pharm Policy Law 16:339-348, 2014
14. Gorlin J: Encouragement of new clinical drug development: The role of data exclusivity. http://www.who.int/intelectualproperty/topics/ip/en/DataExclusivity_2000.pdf
15. Figueroa MI: Precio de los medicamentos en Chile en el contexto de América Latina. Presented at the IMS World Review Conference, Santiago, Chile, May 19, 2016
16. Fiscalía Nacional Económica: Estudio sobre los efectos de la bioequivalencia y la penetración de genéricos en el ámbito de la libre competencia. http://www.dipres.gob.cl/598/articles-168363_recurso_1.pdf
17. Lopes G de L Jr, de Souza JA, Barrios C: Access to cancer medications in low- and middle-income countries. Nat Rev Clin Oncol 10:314-322, 2013
18. Balmaceda C, Espinoza MA, Diaz J: Impacto de una política de equivalencia terapéutica en el precio de medicamentos en Chile. Value Health Reg Issues 8:43-48, 2015
19. Mansilla C, Cárdenas J, Kaplan WA, et al: Evaluation of the effects of a generic substitution policy implemented in Chile. BMJ Glob Health 2:e000922, 2019 (suppl 3)
20. Herrero DS, Castillo C, Ahumada B, et al: Análisis del gasto y mecanismos de compra de medicamentos Del Sistema Nacional de Servicios de Salud. http://www.dipres.gob.cl/598/articles-168363_recursol_1.pdf
21. Ravenós P, Zolezzi S: Electronic tendering of pharmaceuticals and medical devices in Chile. J Bus Res 68:2569-2578, 2015
22. Chile IMS: IMS HealthDatasets: Auditorías de información. Presented at Chilean Ministry of Health, Santiago, Chile, May 2012

Manuscript writing: All authors
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AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO’s conflict of interest policy, please refer to www.asco.org/rcw or ascopubs.org/site/misc/authors.html.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

No potential conflicts of interest were reported.

ACKNOWLEDGMENT
The authors gratefully acknowledge Dominic Hodgkin and Nuria Homedes for their insightful comments; Ista Zahn, from IQSS-Harvard for statistical support; Lorena Hernandez for research assistance; and the Ministry of Health, CENABAST, and INAPI of Chile for providing free access to the datasets.
### Table A1. Drugs Listed in the Cancer Treatment Protocols of the Chilean Ministry of Health, 2012-2017

| Molecule Name     | Health Program | Disease                                           |
|-------------------|----------------|---------------------------------------------------|
| **Allopurinol**   | AUGE           | Pediatric (<15 years of age), lymphoma, leukemia  |
| **Arsenic trioxide** | AUGE         | Leukemia                                          |
| **Asparaginase**  | AUGE           | Leukemia                                          |
| **Bicalutamide**  | AUGE           | Prostate                                          |
| **Bleomycin**     | AUGE           | Pediatric (<15 years of age), ovarian             |
| **Capecitabine**  | AUGE           | Gastric, colorectal                               |
| **Carboplatin**   | AUGE           | Pediatric (<15 years of age), ovarian             |
| **Chlorambucil**  | AUGE           | Leukemia                                          |
| **Cisplatin**     | AUGE           | Cervical, ovarian, bladder                        |
| **Cyclophosphamide** | AUGE         | Lymphoma, leukemia, cervical                      |
| **Cytarabine**    | AUGE           | Lymphoma, leukemia, cervical                       |
| **Dacarbazine**   | AUGE           | Pediatric (<15 years of age)                      |
| **Daclizumab**    | AUGE           | Leukemia                                          |
| **Daunorubicin**  | AUGE           | Lymphoma                                          |
| **Dexamethasone** | AUGE           | Lymphoma, leukemia, cervical, colorectal, bladder |
| **Docetaxel**     | AUGE           | Breast, ovary                                     |
| **Doxorubicin**   | AUGE           | Lymphoma, leukemia                                |
| **Etoposide**     | AUGE           | Gastric, colorectal                               |
| **Filgrastim**    | AUGE           | Lymphoma, leukemia                                |
| **Fludarabine**   | AUGE           | Leukemia                                          |
| **Fluorouracil**  | AUGE           | Breast, colorectal, bladder                       |
| **Flutamide**     | AUGE           | Prostate                                          |
| **Folinato calcium** | AUGE      | Lymphoma, leukemia, cervical, osteosarcoma, colorectal |
| **Gemcitabine**   | AUGE           | Ovarian                                           |
| **Hydrocortisone**| AUGE           | Leukemia                                          |
| **Hydroxycarbamide** | AUGE   | Leukemia                                          |
| **Idarubicin**    | AUGE           | Leukemia                                          |
| **Iflotamid**     | AUGE           | Lymphoma, leukemia, ovarian                       |
| **Imatinib**      | AUGE           | Leukemia                                          |
| **Irinotecan**    | AUGE           | Pediatric (<15 years of age)                      |
| **Lomustine**     | AUGE           | Pediatric (<15 years of age)                      |
| **Mercaptopurine**| AUGE           | Leukemia                                          |
| **Methotrexate**  | AUGE           | Lymphoma, leukemia                                |
| **Mitomycin**     | AUGE           | Bladder                                           |
| **Mitoxantrone**  | AUGE           | Leukemia                                          |
| **Nilotinib**     | AUGE           | Leukemia                                          |
| **Oxaliplatin**   | AUGE           | Colon                                             |

(Continued on following page)
| Molecule Name | Health Program | Disease                           |
|---------------|----------------|-----------------------------------|
| Paclitaxel    | AUGE           | Cervical, ovarian                  |
| Pamidronic acid | AUGE       | Breast, prostate, palliative       |
| Rituximab     | AUGE           | Lymphoma, leukemia                 |
| Tamoxifen     | AUGE           | Breast                            |
| Thalidomide   | AUGE           | Pediatric (< 15 years of age)      |
| Thioguanine   | AUGE           | Leukemia                          |
| Topotecan     | AUGE           | Pediatric (< 15 years of age), ovarian |
| Trastuzumab   | Ricarte Soto   | Breast, gastric                    |
| Tretinoin     | AUGE           | Leukemia                          |
| Vinblastine   | AUGE           | Pediatric (< 15 years of age)      |
| Vincristine   | AUGE           | Pediatric (< 15 years of age) lymphoma, leukemia |

**NOTE.** Adapted from CENABAST dataset, Ministry of Health of Chile.\(^{13,45}\)

Abbreviation: AUGE, Universal Access with Explicit Guarantees.
| Pharmaceutical Companies | Total Observations | Missing Observations | Sources                  |
|---------------------------|--------------------|----------------------|--------------------------|
| 1 Abbott                  | 2,667              | 21                   | IQVIA                    |
| 2 Abbvie                  | 457                | 0                    | IQVIA                    |
| 3 Alcamed                 | 121                | 0                    | CENABAST                 |
| 4 Alapharma               | 9                  | 0                    | CENABAST                 |
| 5 Aspen                   | 95                 | 0                    | IQVIA                    |
| 6 AstraZeneca             | 2,255              | 0                    | IQVIA                    |
| 7 Bristol Myer Squib      | 1,678              | 0                    | IQVIA                    |
| 8 Bago                    | 191                | 0                    | IQVIA                    |
| 9 Baxter                  | 1,764              | 0                    | IQVIA                    |
| 10 Bayer                  | 69                 | 0                    | IQVIA                    |
| 11 Bestpharma             | 427                | 0                    | CENABAST                 |
| 12 Biocross               | 36                 | 36                   | n/a                      |
| 13 Biogen                 | 106                | 0                    | IQVIA                    |
| 14 Biosano                | 1,353              | 0                    | CENABAST, https://www.biosano.cl/pdf/listaPrecios.pdf |
| 15 Biotoscanca            | 19                 | 19                   | n/a                      |
| 16 Boehringer             | 48                 | 1                    | IQVIA                    |
| 17 Chemopharma            | 324                | 0                    | http://www.chemopharma.cl/listadeprecioschemo.pdf |
| 18 Corporacion Nacional del Cancer | 951 | 32 | http://www.conac.cl/botiquin_listado.php |
| 19 Cydpharma              | 63                 | 63                   | n/a                      |
| 20 Deutsche Pharma        | 2                  | 1                    | IQVIA                    |
| 21 Diprovet               | 1                  | 1                    | n/a                      |
| 22 Drog Antofagasta       | 90                 | 90                   | n/a                      |
| 23 Eli Lilly              | 313                | 0                    | IQVIA                    |
| 24 Ethon                  | 1,043              | 0                    | CENABAST                 |
| 25 Eurofarma              | 251                | 84                   | CENABAST, https://www.eurofarma.cl/es/ |
| 26 FCaribean              | 1,951              | 24                   | CENABAST                 |
| 27 FSantiago              | 477                | 0                    | CENABAST                 |
| 28 FSchubert              | 136                | 136                  | n/a                      |
| 29 Ferrer                 | 16                 | 1                    | CENABAST, http://www.ferrerchile.cl/productos/ |
| 30 Ferring                | 4                  | 1                    | IQVIA                    |
| 31 Fresenius              | 7,282              | 191                  | https://www.fresenius-kabi.com/ct/productos/oncologia |
| 32 GDM                    | 72                 | 72                   | n/a                      |
| 33 Glaxo Smithkline       | 544                | 0                    | IQVIA                    |
| 34 Gador                  | 1,339              | 0                    | IQVIA                    |
| 35 Galenicum              | 127                | 0                    | IQVIA                    |
| 36 Gemarkpharma           | 179                | 0                    | IQVIA                    |
| 37 Global Pharma          | 546                | 363                  | CENABAST                 |
| 38 Grunenthal             | 220                | 0                    | CENABAST, https://www.grunenthal.cl/grt-web/Grunenthal_Chilena_Ltda_/171700340.jsp |
| 39 Hospifarma             | 1                  | 1                    | n/a                      |
| 40 Imssipharma            | 2                  | 1                    | CENABAST                 |
| 41 Insuval                | 815                | 548                  | CENABAST                 |
| 42 Janssen                | 596                | 0                    | IQVIA                    |
| 43 Kampar                 | 4,148              | 1                    | IQVIA                    |

(Continued on following page)
| Pharmaceutical Companies | Total Observations | Missing Observations | Sources                      |
|---------------------------|--------------------|----------------------|------------------------------|
| 44 LKM                    | 65                 | 28                   | CENABAST                     |
| 45 Lab. Chile             | 7,635              | 0                    | CENABAST, [https://www.laboratorioc Chile.cl/productos/](https://www.laboratorioc Chile.cl/productos/) |
| 46 Lab. Institucional     | 9                  | 9                    | n/a                          |
| 47 Labonort               | 57                 | 57                   | n/a                          |
| 48 Labvitals              | 237                | 0                    | CENABAST                     |
| 49 Libra                  | 798                | 7                    | CENABAST, [https://www.lablibra.com/libra.php?seccion=principiosactivos&es](https://www.lablibra.com/libra.php?seccion=principiosactivos&es) |
| 50 MSD                    | 373                | 0                    | IQVIA                        |
| 51 Medikar                | 46                 | 46                   | n/a                          |
| 52 Merck Serono           | 243                | 0                    | IQVIA                        |
| 53 Mintlab                | 1                  | 1                    | n/a                          |
| 54 Novartis               | 5,266              | 5                    | IQVIA                        |
| 55 Novofarma              | 48                 | 42                   | CENABAST                     |
| 56 Opko                   | 696                | 0                    | CENABAST                     |
| 57 PMG Pharma             | 98                 | 98                   | n/a                          |
| 58 Pasteur                | 331                | 0                    | IQVIA                        |
| 59 Pentafarma             | 4                  | 4                    | n/a                          |
| 60 Pfizer Chile           | 9,827              | 0                    | IQVIA                        |
| 61 Pharma Investi         | 988                | 0                    | IQVIA                        |
| 62 Pharmamerica           | 115                | 115                  | n/a                          |
| 63 Pharmasan              | 75                 | 0                    | CENABAST                     |
| 64 Pharmatech             | 1,643              | 0                    | IQVIA                        |
| 65 Pharmavisan            | 403                | 350                  | CENABAST                     |
| 66 Qualix                 | 61                 | 61                   | n/a                          |
| 67 Raffo                  | 54                 | 54                   | n/a                          |
| 68 Reutter                | 72                 | 72                   | n/a                          |
| 69 Roche                  | 9,650              | 0                    | IQVIA                        |
| 70 Sanofi                 | 1,342              | 0                    | IQVIA                        |
| 71 Saval                  | 2                  | 2                    | IQVIA                        |
| 72 Seven Pharma           | 27                 | 27                   | n/a                          |
| 73 Sociolfar              | 1                  | 1                    | n/a                          |
| 74 Socofar                | 2,873              | 149                  | CENABAST                     |
| 75 Socosep                | 100                | 100                  | n/a                          |
| 76 Synthon                | 2,573              | 0                    | IQVIA                        |
| 77 Tecnofarma             | 7,407              | 2                    | IQVIA                        |
| 78 Vitasystem             | 3                  | 3                    | n/a                          |
| 79 Winpharm               | 590                | 48                   | n/a                          |
| 80 Zemox                  | 226                | 191                  | CENABAST                     |
| Total                     | 86,727             | 3,158                |                              |

**NOTE.** IQVIA is a company that aggregates data on a drug’s expenditure, former IMS; CENABAST is the public Chilean drug procurement agency. Abbreviation: n/a, not available.
| Molecule Name   | Type of Drug | FDA Approval Date | Target Disease                  | Registered Generic Bioequivalent (2013-2017) | Patent Status in Chile | Total Public Expenditures (2017 US$ millions) | Total Private Expenditures (2017 US$ millions) | Total Expenditures (US$ millions) |
|----------------|--------------|-------------------|---------------------------------|-----------------------------------------------|------------------------|-----------------------------------------------|-----------------------------------------------|----------------------------------|
| Trastuzumab    | Biologic     | 2010              | Breast, gastric                 | 2018                                          | 50.376                 | 2.179                                         | 52.555                                         |                                  |
| Rituximab      | Biologic     | 1997              | Lymphoma                       | Pending                                       | 41.841                 | 1.566                                         | 43.407                                         |                                  |
| Dasatinib      | Small molecule | 2006              | Leukemia                       | 2014                                          | 24.877                 | 2.803                                         | 27.679                                         |                                  |
| Imatinib       | Small molecule | 2001              | Leukemia                       | 2014                                          | 20.257                 | 4.511                                         | 24.768                                         |                                  |
| Triptorelin    | Small molecule | 2001              | Prostate                       |                                               | 20.509                 | 2.762                                         | 23.270                                         |                                  |
| Nilotinib      | Small molecule | 2007              | Leukemia                       | 2008                                          | 17.359                 | 1.004                                         | 18.364                                         |                                  |
| Methotrexate   | Small molecule | 1988              | Osteosarcoma, breast, Hodgkin lymphoma | Yes                                           | 8.162                  | 3.139                                         | 11.301                                         |                                  |
| Filgrastim     | Small molecule | 1998              | Myeloma & bone                 |                                               | 10.129                 | 1.086                                         | 11.215                                         |                                  |
| Glatiramer     | Biologic     | 9.916             |                                 |                                               | 9.916                  | 1.081                                         | 10.996                                         |                                  |
| Capecitabine   | Small molecule | 2001              | Breast, gastric, colorectal     | Yes                                           | 9.386                  | 0.563                                         | 9.949                                          |                                  |
| Goserelin      | Small molecule | 1996              | Breast                         | Abandoned                                     | 9.134                  | 0.434                                         | 9.568                                          |                                  |
| Bevacizumab    | Biologic     | 2004              | Cervical                       |                                               | 6.901                  | 1.552                                         | 8.453                                          |                                  |
| Sirolimus      | Small molecule | 2007              | Ovarian                        |                                               | 6.866                  | 1.326                                         | 8.193                                          |                                  |
| Hydrocortisone | Small molecule | 1952              | Breast                         |                                               | 7.546                  | 0.044                                         | 7.550                                          |                                  |
| Everolimus     | Small molecule | 2009              | Breast                         | Pending                                       | 5.183                  | 1.981                                         | 7.164                                          |                                  |
| Allopurinol    | Small molecule | 2003              | Breast                         | Pending                                       | 3.139                  | 2.154                                         | 5.293                                          |                                  |
| Bortezomib     | Small molecule | 2003              | Lymphoma                       | Yes                                           | 4.575                  | 0.712                                         | 5.287                                          |                                  |
| Oxaliplatin    | Small molecule | 2002              | Colon                          | Yes                                           | 4.339                  | 0.372                                         | 4.712                                          |                                  |
| Leuprolin      | Biologic     | 2000              | Prostate                       |                                               | 2.654                  | 2.045                                         | 4.699                                          |                                  |
| Docetaxel      | Small molecule | 1996              | Breast                         | 2017                                          | 3.645                  | 0.796                                         | 4.441                                          |                                  |
| Gemcitabine    | Small molecule | 1996              | Breast                         |                                               | 3.012                  | 1.109                                         | 4.121                                          |                                  |
| Letrozole      | Small molecule | 2001              | Breast                         | Yes                                           | 1.556                  | 2.328                                         | 3.883                                          |                                  |
| Doxorubicin    | Small molecule | 1999              | Lymphoma                       | Yes                                           | 3.441                  | 0.254                                         | 3.695                                          |                                  |
| Anastrozole    | Small molecule | 1996              | Breast                         | Yes                                           | 1.828                  | 1.536                                         | 3.366                                          |                                  |
| Zoledronic acid| Small molecule | 2001              | Myeloma & bone                 |                                               | 2.410                  | 0.922                                         | 3.332                                          |                                  |
| Pemetrexed     | Small molecule | 2009              | Lung                           | Yes                                           | 1.769                  | 1.559                                         | 3.328                                          |                                  |
| Tamoxifen      | Small molecule | 1977              | Breast                         | Yes                                           | 1.272                  | 1.928                                         | 3.200                                          |                                  |
| Exemestane     | Small molecule | 1999              | Breast                         | Yes                                           | 1.364                  | 1.825                                         | 3.189                                          |                                  |
| Sunitinib      | Small molecule | 2006              | Kidney                         | Rejected                                      | 2.289                  | 0.778                                         | 3.067                                          |                                  |

(Continued on following page)
| Molecule Name  | Type of Drug | FDA Approval Date | Target Disease                  | Registered Generic Bioequivalent (2013-2017) | Patent Status in Chile | Total Public Expenditures (2017 US$ millions) | Total Private Expenditures (2017 US$ millions) | Total Expenditures (US$ millions) |
|---------------|--------------|------------------|---------------------------------|---------------------------------------------|------------------------|-----------------------------------------------|---------------------------------------------|-------------------------------|
| Cetuximab     | Biologic     | 2004             | Colorectal                      | Yes                                         | 2009, pending          | 2.040                                         | 0.957                                       | 2.997                         |
| Paclitaxel    | Small molecule | 2005            | Ovarian, cervical, breast, lung | Yes                                         | 2009, pending          | 2.525                                         | 0.471                                       | 2.996                         |
| Temozolomide  | Small molecule | 1999            | Brain                           | Yes                                         | 2013, pending          | 1.102                                         | 1.693                                       | 2.796                         |
| Irinotecan    | Small molecule | 1998            | Colon                           | Yes                                         | 2013, pending          | 2.427                                         | 0.332                                       | 2.758                         |
| Bicalutamide  | Small molecule | 1973            | Prostate                        | Yes                                         | 2013, pending          | 1.672                                         | 0.919                                       | 2.590                         |
| Lenalidomide  | Small molecule | 2013            | Multiple myeloma                | Yes                                         | 2011, pending          | 1.224                                         | 1.144                                       | 2.367                         |
| Fluorouracil  | Small molecule | 1962            | Skin                            | Yes                                         | 2011, pending          | 1.888                                         | 0.140                                       | 2.028                         |
| Asparaginase  | Biologic     | 2011             | Leukemia                        | Yes                                         | 2013, pending          | 1.924                                         |                               | 1.924                         |
| Natalizumab   | Biologic     | 2004             | n/a                             | Abandoned                                   | Yes                    | 1.755                                         | 0.165                                       | 1.920                         |
| Pazopanib     | Small molecule | 2009            | Kidney                          | Abandoned                                   | Yes                    | 1.329                                         | 0.569                                       | 1.898                         |
| Pamidronate   | Small molecule | 1996            | Myeloma & bone                 | Yes                                         | 2013, pending          | 1.609                                         | 0.130                                       | 1.739                         |
| Golimumab     | Biologic     | 2004             | Tumor                           | Yes                                         | 2013, pending          | 0.484                                         | 1.192                                       | 1.675                         |
| Mercaptopurine| Small molecule | 1953            | Leukemia                        | Yes                                         | 2013, pending          | 1.394                                         | 0.243                                       | 1.638                         |
| Sorafenib     | Small molecule | 2005            | Kidney                          | Rejected                                    | Yes                    | 0.361                                         | 1.238                                       | 1.599                         |
| Abiraterone   | Small molecule | 2011            | Prostate                        | Yes                                         | 2013, pending          | 0.393                                         | 1.117                                       | 1.510                         |
| Erlotinib     | Small molecule | 2004            | Lung                            | Pending                                     | Yes                    | 0.662                                         | 0.824                                       | 1.486                         |
| Azacitidine   | Small molecule | 2004            | Leukemia                        | Yes                                         | 2013, pending          | 1.349                                         | 0.092                                       | 1.441                         |
| Dexamethasone | Small molecule | 2009            | Leukemia                        | Yes                                         | 2013, pending          | 1.368                                         | 0.000                                       | 1.368                         |
| Cyclophosphamide | Small molecule | 1999           | Leukemia                        | Yes                                         | 2013, pending          | 1.246                                         | 0.105                                       | 1.351                         |
| Cytarabine    | Small molecule | 1999            | Leukemia                        | Yes                                         | 2013, pending          | 1.255                                         | 0.053                                       | 1.307                         |
| Flutamide     | Small molecule | 1996            | Prostate                        | Yes                                         | 2013, pending          | 1.358                                         | 0.000                                       | 1.358                         |
| Carboplatin   | Small molecule | 1989            | Ovarian                         | Yes                                         | 2013, pending          | 1.358                                         | 0.000                                       | 1.358                         |
| Thalidomide   | Small molecule | 1998            | Myeloma & bone                 | Yes                                         | 2013, pending          | 1.358                                         | 0.000                                       | 1.358                         |
| Hydroxyurea   | Small molecule | 1967            | Leukemia, cervical              | Yes                                         | 2013, pending          | 1.358                                         | 0.000                                       | 1.358                         |
| Tretinoin     | Small molecule | 1995            | Leukemia                        | Yes                                         | 2013, pending          | 1.358                                         | 0.000                                       | 1.358                         |
| Enzalutamide  | Small molecule | 2012            | Prostate                        | Yes                                         | 2013, pending          | 1.358                                         | 0.000                                       | 1.358                         |
| Cisplatin     | Small molecule | 1978            | Testicular, ovarian, cervical, breast, bladder | Yes | 2013, pending | 1.358                                         | 0.000                                       | 1.358                         |

(Continued on following page)
| Molecule Name |Type of Drug |FDA Approval Date |Target Disease |Registered Generic Bioequivalent (2013-2017) |Patent Status in Chile |Registered Data Exclusivity |Total Public Expenditures (2017 US$ millions) |Total Private Expenditures (2017 US$ millions) |Total Expenditures (US$ millions) |
|---------------|-------------|------------------|---------------|---------------------------------------------|----------------------|---------------------------|---------------------------------------------|---------------------------------------------|------------------------------------------|
| Ipilimumab    |Biologic    |2011              |Skin           |                                             |                      |                           |0.663                                        |0.398                                        |1.061                                     |
| Fluorouracil  |Small molecule| 1991              |Leukemia      |                                             |                      |                           |0.834                                        |0.053                                        |0.887                                     |
| Ifosfamide    |Small molecule| 1988              |Testicles     |Yes                                         |                      |                           |0.823                                        |0.021                                        |0.844                                     |
| Idarubicin    |Small molecule| 1990              |Leukemia      |Yes                                         |                      |                           |0.795                                        |0.030                                        |0.825                                     |
| Fulvestrant   |Small molecule| 2002              |Breast         |                                             |                      |                           |0.356                                        |0.376                                        |0.732                                     |
| Melphalan     |Small molecule| 1964              |Myeloma & bone |                                             |                      |                           |0.621                                        |0.077                                        |0.697                                     |
| Daunorubicin  |Small molecule| 1979              |Leukemia      |                                             |                      |                           |0.664                                        |0.002                                        |0.666                                     |
| Cladribine    |Small molecule| 2016              |Leukemia      |                                             |                      |                           |0.594                                        |—                                            |0.594                                     |
| Axitinib      |Small molecule| 2012              |Kidney         |                                             |                      |                           |0.427                                        |0.164                                        |0.592                                     |
| Bleomycin     |Small molecule| 1973              |Leukemia      |                                             |                      |                           |0.508                                        |0.056                                        |0.565                                     |
| Vincristine   |Small molecule| 1963              |Leukemia      |2011                                        |                      |                           |0.406                                        |0.152                                        |0.557                                     |
| Carmustine    |Small molecule| 1997              |Lymphoma, myeloma, brain tumors|                                             |                      |                           |0.519                                        |—                                            |0.519                                     |
| Ruxolitinib   |Small molecule| 2011              |Bones         |Pending                                      |                      |                           |0.279                                        |0.226                                        |0.504                                     |
| Afatinib      |Small molecule| 2013              |Lung          |                                             |                      |Yes                        |0.174                                        |0.324                                        |0.498                                     |
| Hydroxyurea   |Small molecule| 1967              |Leukemia      |Yes                                         |                      |                           |0.428                                        |—                                            |0.428                                     |
| Etoposide     |Small molecule| 1994              |Lung          |                                             |                      |                           |0.402                                        |0.021                                        |0.423                                     |
| Thiopeta      |Small molecule| 1959              |Breast, ovarian, bladder, lymphoma|                                             |                      |                           |0.411                                        |0.010                                        |0.421                                     |
| Cabazitaxel   |Small molecule| 2010              |Prostate      |                                             |                      |Yes                        |0.304                                        |0.078                                        |0.382                                     |
| Plerixafor     |Small molecule| 2008              |Leukemia      |Yes                                         |                      |                           |0.272                                        |0.044                                        |0.316                                     |
| Dactinomycin  |Small molecule| 1975              |Skin, lymphoma|Yes                                         |                      |                           |0.291                                        |0.014                                        |0.306                                     |
| Regorafenib   |Small molecule| 2012              |Colorectal    |Pending                                      |                      |                           |0.188                                        |0.305                                        |0.305                                     |
| Ixabepilone   |Small molecule| 2007              |Breast        |                                             |                      |                           |0.206                                        |0.098                                        |0.304                                     |
| Arsenic trioxide | Small molecule| 2000              |Leukemia      |                                             |                      |                           |0.296                                        |—                                            |0.296                                     |
| Vemurafenib   |Biologic     |2011              |Skin          |Yes                                         |                      |                           |0.263                                        |0.033                                        |0.295                                     |
| Nivolumab     |Biologic     |2014              |Skin          |Yes                                         |                      |                           |0.102                                        |0.170                                        |0.272                                     |
| Trastuzumab emtansine | Biologic| 2013              |Breast        |Yes                                         |                      |                           |0.202                                        |0.066                                        |0.268                                     |
| Bendamustine  |Small molecule| 2008              |Leukemia      |Yes                                         |                      |                           |0.200                                        |0.049                                        |0.249                                     |
| Dactinomycin  |Small molecule| 1964              |Myeloma & bone|                                             |                      |                           |0.224                                        |0.004                                        |0.228                                     |

(Continued on following page)
| Molecule Name | Type of Drug | FDA Approval Date | Target Disease | Generic (2013-2017) | Bioequivalent (2013-2017) | Patent Status in Chile | Registered Data Exclusivity (2013-2017) | Total Public Expenditures (2017 US$ millions) | Total Private Expenditures (2017 US$ millions) | Total Expenditures (US$ millions) |
|---------------|--------------|-------------------|---------------|---------------------|-------------------------|------------------------|--------------------------------|----------------------------------|------------------------------------------|-------------------------------|
| Pertuzumab    | Biologic     | 2012              | Breast        | Yes                 | 0.214                   | 0.004                  | Expired                       | 0.218                             | 0.218                                   | 0.218                        |
| Interferon alfa-2B | Biologic     | 1997              | Skin          |                     | 0.196                   | 0.026                  | Expired                       | 0.202                             | 0.202                                   | 0.202                        |
| Epirubicin    | Small molecule | 1999            | Breast        |                     | 0.090                   | 0.107                  | Expired                       | 0.198                             | 0.198                                   | 0.198                        |
| Palbociclib   | Small molecule | 2003              | Breast        | Yes                 | 0.066                   | 0.191                  | Expired                       | 0.190                             | 0.190                                   | 0.190                        |
| Crizotinib    | Small molecule | 2011              | Lung          |                     | 0.134                   | 0.057                  | Expired                       | 0.187                             | 0.187                                   | 0.187                        |
| Vinorelbine   | Small molecule | 1994              | STomach       |                     | 0.134                   | 0.053                  | Expired                       | 0.187                             | 0.187                                   | 0.187                        |
| Miconycin     | Small molecule | 1997              | Breast        | Yes                 | 0.156                   | 0.014                  | Expired                       | 0.169                             | 0.169                                   | 0.169                        |
| Vinblastine   | Small molecule | 1964              | Skin          |                     | 0.146                   | 0.148                  | Expired                       | 0.164                             | 0.164                                   | 0.164                        |
| Lipidinib     | Biologic     | 2002              | Breast        |                     | 0.092                   | 0.102                  | Expired                       | 0.114                             | 0.114                                   | 0.114                        |
| Pentostatinib | Small molecule | 2003              | Skin          |                     | 0.032                   | 0.120                  | Expired                       | 0.122                             | 0.122                                   | 0.122                        |
| Lutetinib     | Small molecule | 1997              | Leukemia      |                     | 0.054                   | 0.075                  | Expired                       | 0.119                             | 0.119                                   | 0.119                        |
| Chlorambucil  | Small molecule | 1987              | Prostate      |                     | 0.132                   | 0.077                  | Expired                       | 0.139                             | 0.139                                   | 0.139                        |
| Mitoxantrone  | Small molecule | 1987              | Prostate      |                     | 0.132                   | 0.077                  | Expired                       | 0.139                             | 0.139                                   | 0.139                        |
| Trabectedin   | Small molecule | 2015              | Lung          |                     | 0.054                   | 0.085                  | Expired                       | 0.119                             | 0.119                                   | 0.119                        |
| Secukinumab   | Biologic     | 2015              | Skin          |                     | 0.071                   | 0.042                  | Expired                       | 0.113                             | 0.113                                   | 0.113                        |
| Bevacizumab   | Small molecule | 2000              | Skin          |                     | 0.113                   | 0.042                  | Expired                       | 0.113                             | 0.113                                   | 0.113                        |
| Folinic acid  | Small molecule | 2008              | Colorectal    |                     | 0.112                   | 0.111                  | Expired                       | 0.111                             | 0.111                                   | 0.111                        |
| Eribulin      | Small molecule | 2013              | Breast        |                     | 0.108                   | 0.118                  | Expired                       | 0.118                             | 0.118                                   | 0.118                        |
| Temsirolimus  | Small molecule | 2001              | Kidney        |                     | 0.098                   | 0.099                  | Expired                       | 0.099                             | 0.099                                   | 0.099                        |
| Thioguanine   | Small molecule | 1966              | Leukemia      |                     | 0.098                   | 0.094                  | Expired                       | 0.093                             | 0.093                                   | 0.093                        |
| Lomustine     | Small molecule | 1976              | Brain         |                     | 0.095                   | 0.095                  | Expired                       | 0.095                             | 0.095                                   | 0.095                        |
| Clofarabine   | Small molecule | 2004              | Leukemia      |                     | 0.095                   | 0.095                  | Expired                       | 0.095                             | 0.095                                   | 0.095                        |
| Brentuximab   | Small molecule | 2011              | Lymphoma      |                     | 0.094                   | 0.094                  | Expired                       | 0.094                             | 0.094                                   | 0.094                        |
| Ohnurazumab   | Small molecule | 2011              | Lymphoma      |                     | 0.094                   | 0.094                  | Expired                       | 0.094                             | 0.094                                   | 0.094                        |
| Degutecix     | Small molecule | 2010              | Prostate      |                     | 0.094                   | 0.094                  | Expired                       | 0.094                             | 0.094                                   | 0.094                        |
| Basilixib     | Small molecule | 2006              | Leukemia      |                     | 0.095                   | 0.095                  | Expired                       | 0.095                             | 0.095                                   | 0.095                        |
| Denileukin    | Small molecule | 2005              | Lymphoma      |                     | 0.095                   | 0.095                  | Expired                       | 0.095                             | 0.095                                   | 0.095                        |
| Vorinostat    | Small molecule | 2006              | Lymphoma      |                     | 0.095                   | 0.095                  | Expired                       | 0.095                             | 0.095                                   | 0.095                        |
| Molecule Name       | Type of Drug | FDA Approval Date | Target Disease     | Registered Generic Bioequivalent (2013-2017) | Patent Status in Chile | Registered Data Exclusivity | Total Public Expenditures (2017 US$ millions) | Total Private Expenditures (2017 US$ millions) | Total Expenditures (US$ millions) |
|---------------------|-------------|------------------|-------------------|---------------------------------------------|------------------------|----------------------------|---------------------------------------------|-------------------------------------------|----------------------------------|
| Procarbazine        | Small molecule | 1969             | Lymphoma, brain   |                                             |                         |                            | 0.029                         | 0.029                                     | 0.029                             |
| Cobimetinib         | Biologic     | 2015             | Skin              | Yes                                         | —                      |                            | 0.023                         | 0.023                                     | 0.023                             |
| Medroxyprogesterone | Small molecule | 1995             | Breast            |                                             | 0.013                  |                            | 0.009                         | 0.022                                     | 0.022                             |
| Vismodegib          | Small molecule | 2012             | Skin              |                                             | 0.018                  |                            | 0.018                         |                                          | 0.018                             |
| Lenograstim         | Biologic     | 1998             | Ovarian           |                                             | 0.014                  |                            | 0.001                         | 0.015                                     | 0.015                             |
| Belatacept          | Biologic     | 2011             | Prevent organ rejection |                                     | 0.013                  |                            | 0.013                         |                                          | 0.013                             |
| Estramustine        | Small molecule | 1981             | Prostate          |                                             | 0.001                  |                            | 0.012                         | 0.013                                     | 0.013                             |
| Pomalidomide        | Small molecule | 2013             | Myeloma & bone    | 2019                                        | —                      | 0.007                      | 0.000                         | 0.007                                     | 0.007                             |
| Megestrol           | Small molecule | 2019             | Palliative        |                                             | 0.007                  |                            | 0.000                         |                                          | 0.007                             |
| Mitotane            | Small molecule | 1960             | Adrenocortical carcinoma |                                     | 0.006                  |                            | 0.000                         |                                          | 0.006                             |
| Ramucirumab         | Biologic     | 2014             | Gastric           | Yes                                         | —                      | 0.005                      | 0.005                         |                                          | 0.005                             |
| Dabrafenib          | Small molecule | 2013             | Advanced melanoma | Yes                                         | —                      | 0.005                      | 0.005                         |                                          | 0.005                             |
| Teniposide          | Small molecule | 1992             | Leukemia children |                                             | 0.005                  |                            | 0.000                         |                                          | 0.005                             |
| Peginterferon alfa-2b | Biologic   | 2011             | Skin              |                                             | —                      | 0.004                      | 0.004                         |                                          | 0.004                             |
| Trametinib          | Small molecule | 2013             | Skin              |                                             | —                      | 0.003                      | 0.003                         |                                          | 0.003                             |

NOTE. Adapted from DrugBank,27 CenterWatch,28 National Cancer Institute,46 INAPI dataset, and CENABAST dataset. Abbreviation: FDA, Food and Drug Administration.