

ACCESS TO CANCER TREATMENT

A study of medicine pricing issues with recommendations for improving access to cancer medication

A report prepared for OXFAM

By Ellen 't Hoen, LL.M. - Medicines Law & Policy.

ABSTRACT

According to the World Health Organization (WHO), cancer is one of the leading causes of death in the world, with 8.2 million deaths in 2012. More than 60 percent of the world's total new annual cases occur in Africa, Asia, and Central and South America. These regions account for 70 percent of the world's cancer deaths. In low- and middle-income countries, treatment for cancer is not widely available. Health systems are often not equipped to deal with detection and treatment of cancers. Prevention and early detection programmes are often weak or non-existent. This situation is exacerbated in some cases by the high cost of treatment and in particular the high cost of newer cancer medication. The unsustainability of cancer medication pricing has increasingly become a global issue creating access challenges in low- and middle-income but also high-income countries. This report describes recent developments with pricing of medicines for the treatment of cancer, discusses what lessons can be drawn from HIV/AIDS treatment scale up and makes some recommendations to help increase access to treatment for people with cancer.

This research report was written to share research results, to contribute to public debate and to invite feedback on development and humanitarian policy and practice. It does not reflect Oxfam policy positions. The views expressed are those of the author and not those of Oxfam.

Acknowledgements

I would like to thank Mohga Kamal-Yanni and Philippa Saunders from Oxfam UK for their guidance throughout the project and Stephanie Burgos from Oxfam America for providing useful comments on earlier versions of the report. I thank Joseph Kaiwood for his assistance in the background research on access policies of pharmaceutical companies. I thank Krisantha Weerasurya and Peter Beyer from the World Health Organization for providing information and introductions to useful contacts. David Banta M.D. provided useful research on specific diseases and reviewed medical information used in the report. I am thankful to many others who have responded to my queries throughout this project. I would especially like to mention Leena Menghaney and Aastha Gupta for information about medicine pricing and policy in India. I am immensely grateful to the external reviewers, Niranjana Kondori from Management Sciences for Health, Rohit Malpani from Médecins sans Frontières and Marg Ewen from Health Action International, whose thoughtful comments, suggestions and corrections were essential to produce the final result.

Ellen 't Hoen
Paris, 2 May 2014

Table of Contents

1	Introduction	4
2	Pricing of medicines	5
	MEDICINE PRICING ISSUES IN HIGH-INCOME COUNTRIES.....	5
	HOW ARE DRUG PRICES SET?	8
3	Cancer and cancer medicine pricing	12
	CANCER CARE IN INDIA.....	13
	PRICES OF SELECTED ESSENTIAL CANCER DRUGS IN LOW- AND MIDDLE-INCOME COUNTRIES.....	13
	CASES OF SPECIFIC CANCER DRUGS	15
	<i>Trastuzumab - Roche (breast cancer)</i>	16
	<i>Letrozole (Femara)– Novartis (breast cancer)</i>	18
	<i>Imatinib mesylate (Gleevec) – Novartis (CML)</i>	19
	<i>Dasatinib (Sprycel) – Bristol-Myers Squibb (CML)</i>	22
	<i>Docetaxel (Taxotere) – Sanofi-Aventis (breast cancer)</i>	24
4	Lessons from HIV and pricing of ARVs	25
	MARKET FOR CANCER DRUGS.....	25
	GENERIC COMPETITION	26
	SMALL MOLECULES VS. BIOLOGICS – REGULATORY CHALLENGES.....	27
	WHO MODEL LIST OF ESSENTIAL MEDICINES	27
	PROCUREMENT ISSUES AND PRICE TRANSPARENCY.....	28
	POLITICAL ENVIRONMENT	29
	FINANCING OF HIV VERSUS FINANCING OF CANCER CARE.....	30
	CONCLUSION	30
5	Pharmaceutical companies’ access policies for cancer drugs in low- and middle-income countries.....	30
	ROCHE	31
	NOVARTIS.....	32
	SANOFI-AVENTIS.....	33
	BRISTOL-MYERS SQUIBB.....	34
	BAYER.....	35
	CONCLUSION	35
6	Country strategies aimed at decreasing the prices of cancer drugs.....	36
	INDIA	37
	<i>Compulsory licensing of cancer drugs</i>	37
	<i>Cases of patent grant opposition for cancer drugs</i>	38
	<i>Responses from industry – fierce response from US</i>	38
	THAILAND	38
	<i>Compulsory licensing for cancer drugs</i>	38
	<i>Effects on export trade and foreign direct investment</i>	40
7	Conclusions and recommendations	41
	SPECIFIC RECOMMENDATION TO IMPROVE ACCESS TO CANCER MEDICINES	45

1 INTRODUCTION

According to the World Health Organization (WHO), cancer is one of the leading causes of death in the world, with 8.2 million deaths in 2012.¹ Lung, female breast, colorectal, and stomach cancers were the most commonly diagnosed cancers: more than 40 percent of all cancers. Lung, stomach, liver, colon and breast cancer cause the most deaths. While cancer is often categorized as a non-communicable disease (NCD), 20 percent of cancer deaths in low- and middle-income countries are linked to viral infections such as hepatitis and human papilloma virus (HPV).² Infection-related cancers in Sub-Saharan Africa account for 33 percent and in China for 27 percent.³

While death rates from cancer in wealthy countries are slightly declining because of early diagnosis and the availability of treatment, this is not the case in low- and middle-income countries. The rates are rising in low- and middle-income countries, partly because of the aging of the population. Currently 14 million people a year are diagnosed with cancer. That will increase to 19 million by 2025, 22 million by 2030 and 24 million by 2035. More than 60 percent of the world's cancer cases occur in Africa, Asia, and Central and South America.⁴

Some of the common cancer types such as breast cancer, cervical cancer, oral cancer, and colorectal cancer respond well to treatment when detected early. Some cancer types, such as leukaemia and lymphoma in children and testicular seminoma, can be cured provided the appropriate treatment is given, even when disseminated.

In low- and middle-income countries, however, treatment for cancer is not widely available. According to the Global Task Force on Expanded Access to Cancer Care and Control, only 5 percent of global resources for cancer are spent in the developing world, yet these countries account for almost 80 percent of disability-adjusted years of life⁵ lost to cancer globally.⁶

Health systems are often unable to deal with cancer treatment. Prevention and early detection programmes are weak or non-existent. This situation is exacerbated by the lack of financing for healthcare and low health insurance and social security coverage. In low-income countries, the lack of resources requires prioritization of life-saving treatments with high public health impact over cancer care. In certain cases, the high cost of treatment and in particular the high cost of cancer medication throws up additional barriers.

This report will describe recent trends in the pricing of medicines for the treatment of cancer, it will discuss what lessons can be drawn from dramatic price reductions of antiretrovirals (ARVs) and subsequent HIV/AIDS treatment scale up, and make some recommendations to help increase access to treatment for cancer medications, with a particular emphasis on India. India is a particular focus of the report because it is an important lower middle-income country with large unmet needs in cancer care and it has considerable production capacity and potential to produce low-cost medications. Some states in India have announced programmes to provide free medicines to its

population. The first compulsory patent license for a cancer drug was granted by India. The report also looks at price developments in the US. The US is an important innovator in the cancer field and has the highest expenditure for health per capita in the world. But the cost of new cancer medications is creating problems for those US citizens who pay out-of-pocket – even for those who only pay partially as well as for health insurance.

2 PRICING OF MEDICINES

Setting of a price is a function of the affordability of the society in which we work. Simply because we have a patent or simply because we have data exclusivity doesn't suddenly make the population rich. These are two different issues and industry needs to be wise and thoughtful or else the bargain will be destroyed or never consummated in the developing countries.

Sir Andrew Witty, CEO GlaxoSmithKline, 2011⁷

The unsustainability of high prices of new medicines is increasingly becoming an issue of global concern. In developing countries, governments and individuals struggle to pay for products that are priced at several times the level of their per capita GDP.⁸ Particularly in a situation where the product has no competitors, buyers are at the mercy of a single provider, often the patent holder of the product. The high prices of new medicines and in particular those to treat potentially fatal diseases, also receive much attention in high-income countries. Prices of new cancer medication, for example, rise at a higher rate than public and private spending on healthcare, creating challenges even for health systems and individuals in high-income countries. Cancer drug prices have doubled in the US in the last decade from an average of \$5,000 a month to \$10,000.⁹

The problem of high drug prices has received a great deal of attention in the area of HIV/AIDS because life-saving antiretroviral treatments were priced out-of-reach of people and their communities in developing countries. But the high drug price problem is by no means confined to HIV/AIDS as is illustrated by the recent legal battles over cancer medications in India.¹⁰ Nor is it confined to developing countries. The high price of cancer drugs in particular is increasingly the subject of harsh criticism by consumers and the medical profession globally.^{11,12,13}

Medicine pricing issues in high-income countries

The US has the highest prescription drug prices in the world. Many patients there pay a considerable part of the cost of treatment out of pocket. High drug prices were responsible for 50 million Americans skipping medication in 2012.¹⁴ Nearly half of American adults were reported in 2012 to be either without coverage part of the time or permanently underinsured. Lack of healthcare coverage is an important concern for US citizens who are confronted with a serious illness. Medical cost was the cause of 62 percent of all personal bankruptcies filed in the US in 2007.¹⁵ In particular the cost of cancer drugs has been a concern.

One reason for this concern is the rising cost of medication in Medicare. Spending on 'part B drugs', a category dominated by anticancer drugs, rose from \$3bn in 1997 to \$11bn in 2004.¹⁶ Even for those individuals that benefit from healthcare coverage, such as Medicare, the cost of certain cancer drugs can be hugely problematic because of co-payment by the patient. Oncologists of the Memorial Sloan-Kettering Cancer Center described the consequences of an \$11,000 a month price tag for the colorectal cancer drug Zaltrap (ziv-aflibercept), which is marketed in the US by Sanofi and Regeneron. The monthly out of pocket cost for the typical Medicare patient is \$2,200 in co-payment, which is more than the monthly income of half of the Medicare patients. In other words prescribing this drug would mean leaving half of the patients and often their families without money to live on. In an op-ed in the New York Times, three oncologists took a public stand not to prescribe the drug and to opt for a less costly and equally effective treatment instead.¹⁷ Following the publicity of this announcement, Sanofi swiftly lowered the price of Zaltrap by 50 percent. This reduction brought the price closer to the price level of its competitor product Avastin at \$5,000 a month, which is still a hefty price.

As recently as May 2013 a group of over 100 experts in chronic myeloid leukaemia (CML) published an editorial in *Blood* drawing attention to the effects of high cancer drug prices for patients and the healthcare system. They highlight the case of Novartis's product Gleevec (imatinib), which today comes with a price tag in the US of \$92,000 per year. The authors point out that the development cost has long been earned back by the company and that the number of patients using imatinib continues to rise, which should lead to a reduction in price. Instead, since the introduction of imatinib in the US in 2001, the price has nearly tripled.¹⁸

Box 1 – Call for action on cancer drug prices

In April 2013, 100 experts in chronic myeloid leukaemia (CML) raised the alarm about the high prices being charged for new cancer drugs. They stated that the unsustainably high prices harm patients. They proposed a dialogue to find solutions to high prices. They called for immediate action when they wrote:

'As physicians, we follow the Hippocratic Oath of "Primum non nocere", first (or above all) do no harm. We believe the unsustainable drug prices in CML and cancer may be causing harm to patients. Advocating for lower drug prices is a necessity to save the lives of patients who cannot afford them. Pricing of cancer and other drugs involves complex societal and political issues which demand immediate attention, and which will need to consider many factors and involve many constituencies: FDA and governmental regulators; changes in legislation; patent laws; multitudes of regulatory agencies in the US and internationally; offices of human research protection (OHRP); impediments by lawyers and contract research organizations (CROs) which increase the cost of clinical research; patient advocacy groups; excessive regulation and bureaucracy; profits of physicians and hospitals/pharmacies; insurance companies; pharmaceutical companies; etc... We propose to begin the dialogue by organizing regular meetings, involving all parties concerned, to

*address the reasons behind high cancer drug prices and offer solutions to reduce them. For CML, and for other cancers, we believe drug prices should reflect objective measures of benefit, but should also not exceed values that harm our patients and societies.*¹⁹

In the United States, where HIV treatment comes with a price tag of \$20,000 per year, waiting lists exist for state HIV drug assistance. In 2012, 2,000 people remained on such lists. It is anticipated that once the patent term of HIV medications expires in the US, HIV treatment will become available for as little as \$200 per patient per year.²⁰

The high prices of new HIV medication spurred a citizens' initiative in San Francisco called the 'Stop Runaway Drug Pricing' initiative, which aims at giving local government officials the power to negotiate the cost of essential medicines for various public health programmes. The initiative had collected sufficient signatures for the proposal to pass with an 80 percent majority at local elections on 5 November 2013.^{21,22}

In Western Europe the public has largely been protected from the high cost of pharmaceutical care because the financing of healthcare does not fall on individuals. However, the economic crisis and subsequent austerity measures have put the spotlight on the fact that prices of new medicines have also become unsustainable in Europe.²³ The consequences of high drug prices are most painfully felt in cancer care. In 2011 Roche stopped the supply of cancer drugs and other medicines to Greek state hospitals because of unpaid bills. Roche is the world's largest maker of cancer drugs with \$20.6bn in annual sales. (The Greek healthcare budget in 2011 was €6bn (approx. \$8.3bn)²⁴) Novo Nordisk had done the same for insulin.²⁵

The more affluent European countries also struggle with the high cost of medicines. In 2012 the Dutch College for Health Insurance initially recommended excluding three medicines for the treatment of the rare diseases, Pompe and Fabry diseases, because they had become too expensive. Pompe disease is an inherited disorder caused by the build up of a complex sugar called glycogen in the body's cells which impairs certain organs and tissues, especially muscles, from functioning normally.²⁶ Fabry disease is caused by the lack of, or faulty, enzyme needed to metabolize lipids. Symptoms usually begin during childhood or adolescence and include burning sensations in the hands that get worse with exercise and hot weather and small raised reddish-purple blemishes on the skin. Lipid storage may lead to impaired arterial circulation and increased risk of heart attack or stroke. The heart may also become enlarged and the kidneys may become progressively involved. Other signs include decreased sweating, fever, and gastrointestinal difficulties.²⁷ These diseases affect small numbers of patients in the Netherlands (Pompe 100 patients, Fabry 40–50) but the treatment costs are in the millions each year (€44m (\$49m) for Pompe and €11m (\$12) for Fabry).²⁸

This news sparked a national debate on the reimbursement of medicine costs and the role of the pharmaceutical industry in the development and pricing of the products.

The chair of the board of the Erasmus Medical Centre in Rotterdam has called on the government to set up a not-for-profit R&D consortium for rare diseases in the EU to ensure the development of treatments for rare diseases and decrease dependency on the pharmaceutical industry.²⁹ Dr H. Schellekens, Professor of medical biotechnology at the University of Utrecht and member of the Dutch medicines board, called for a radical overhaul of the innovation system, and suggested abolishing pharmaceutical patents to use the savings to invest in R&D directly.³⁰

In the UK some National Health Service trusts have denied patients innovative cost-effective treatments recommended by NICE because they considered them too expensive. This included, for example, the cancer medication erlotinib.³¹ NICE chairman Sir Michael Rawlins has called the refusal to offer patients NICE-endorsed treatments unlawful and encouraged patients to seek relief in court.³²

How are drug prices set?

The swift response by Sanofi, which dropped the price of Zaltrap by 50 percent in response to the criticism of influential oncologists in the *New York Times* illustrates the mysterious ways of price setting by pharmaceutical companies. There seems to be no link between production cost and price. The actual production cost of a product can be very low, as is shown when a patent expires and generic manufacturers enter the market, when price reductions of 99 percent can occur. The mark-ups are well above marginal cost of production, meaning the profit can be huge, in particular if the company dominates the market, as in the case of patent holders. One example is sofosbuvir, a new oral treatment for hepatitis C which can be manufactured for \$68–136 per 12-week course but comes with a list price of \$80,000 for a 12 week treatment course.³³ Nor does there seem to be a connection between medical value and price. Sorafenib sold by Bayer as Nexavar is a cancer medication indicated for advanced liver cancer that may extend life by three months but costs \$80,000 for a 10-month course. For kidney cancer the average price is \$96,000 per year and it needs to be taken for five years. In India, Bayer's patented sorafenib price was approximately \$5,551 for one month's treatment. The Indian generic producer NATCO makes a generic version of sorafenib for \$177,^{34,35} which brings the average cost for a 10-month course of liver cancer treatment to \$1770 and for a five-year treatment course for kidney cancer to \$10,620.

Originator companies explain their pricing strategies by the need to generate resources to invest in the R&D of new products. According to the industry, it costs \$1.2bn in R&D expenses to bring a drug to market.³⁶ However, there is insufficient transparency about drug companies' R&D costs to allow a blind acceptance of that assertion. Andrew Witty, CEO of GlaxoSmithKline, called this \$1bn figure, 'one of the great myths of the industry.'³⁷ An analysis of pharmaceutical R&D expenditure by Light and Warburton published in *Biosocieties*, concluded that the median R&D cost for a company was around \$56m per drug.³⁸ Best estimates of Novartis' R&D expenditure towards the

development of Gleevec (imatinib) are between \$38m and \$96m. The sales for Novartis' Gleevec in 2012 were \$4.675bn, or \$390m per month.³⁹ (See also section 2.1.2.)

Table 1 – Sales of the 10 leading companies in the global cancer market 2010* and 13 best selling cancer drugs⁴⁰ (*Global oncology sales by the pharmaceutical industry accounted for \$61.45bn in 2012 and is expected to rise to \$81.30bn in 2018.⁴¹)

Company	Annual sales Cancer drugs \$ (2010)	Most important Products of the top 5 companies	Comments
Roche	20.6bn	Avastin (bevacizumab) Herceptin (trastuzumab) MabThera (rituximab) Xeloda (capecitabine) Tarceva (erlotinib)	The top 3 products account for 79% of sales in Roche's cancer portfolio.
Novartis	4.3bn	Gleevec (imatinib)	Gleevec accounts for 68% of Novartis' cancer portfolio.
AstraZeneca	4bn	Arimidex (anastrozole)	This product accounts for 38.5% of AstraZeneca's cancer drug sales. Arimidex a hormonal post-surgical treatment for breast cancer in postmenopausal women – recommended by NICE in 2009 for estrogen positive breast cancer.
Sanofi-Aventis	3.4bn	Taxotere (docetaxel) Eloxatine (oxaliplatin)	Taxotere ,a drug to treat breast, ovarian and non-small cell lung cancer, accounts for 80% of Sanofi-Aventis's cancer sales. Eloxatine indication: colorectal cancers.
Eli Lilly	3.4bn	Alimta (pemetrexed) Gemzar (gemcitabine) Erbix (cetuximab)	Alimta is used to treat- asbestos-induced mesothelioma, lung cancers.
Pfizer	2.1bn		
Johnson & Johnson	2.0bn	Velcade (bortezomib)	
Takeda	1.9bn		
Bristol-Myers Squibb	1.7bn		
Merck & co	1.3bn		
Total top 10	46bn		

By comparison, if one looks at the R&D costing figures of not-for-profit drug developers, significant innovations seem possible for only a fraction of the expenditure on R&D by commercial companies.

The October 2001 report by the Global Alliance for Tuberculosis Drug Development, entitled 'The Economics of TB Drug Development', estimated the costs of successfully developing a new chemical entity (NCE) to treat TB to be approximately \$36.8m– \$39.9m (U.S. costs, excluding costs of failure). This estimated range covers preclinical development (\$4.9 m–\$5.3m), pharmaceutical development (at least \$5.3m), and Phases I through III of clinical development (\$26.6m). If one includes the estimated cost of unsuccessful projects the estimated costs of developing an NCE are approximately \$76m–\$115m.⁴²

More recent data is provided by the Drugs for Neglected Diseases initiative (DNDi). The DNDi estimates that the R&D expenditure for an improved treatment (combination product with existing compounds) is between €6m and €20m (approx. \$8.3m–\$27m) and €30m–€40m (approx. \$41m–\$55m) for the

full development of an NCE. These figures do not include contributions in kind from partners. If one applies standard attrition for the DNDi products, the DNDi's cost for the development of an NCE is estimated to be €100m–150m. (\$112m – 169m) These estimates are based on real cost for products that have been developed, or are under development, by the DNDi.⁴³

In conclusion, the cost of new drug development as an explanation for the high prices of new medicines is not convincing. A more likely explanation is that companies charge what the market can bear. And when it comes to healthcare and certainly in the case of potentially fatal diseases such as cancer, people are willing to bear a heavy burden even if the health benefits in reality turn out to be limited.

It should be recognized that investment by governments in the research and development of cancer medicines is substantial and that such public funding is important in the development of new medicines. In 2011, Ashley Stevens et al. published an analysis of 40 years of public sector research contributions to biomedical R&D. They found that 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through research carried out in public sector research institutions. These drugs included 93 small-molecule drugs, 36 biologic agents, 15 vaccines, eight *in vivo* diagnostic materials, and one over-the-counter drug. More than half of these drugs have been used in the treatment or prevention of cancer or infectious diseases. Public sector research was involved in 19 percent of the new drugs that received priority review status by the FDA, indicating the importance of such products.⁴⁴

Table 2 – FDA-Approved drugs discovered through public-sector research, according to type of review and chemical type, 1990–2007

Type of Review	New Molecular Entity	New Ester, Salt, or Derivative	New Formulation	New Combination	New Manufacturer	New Indication	Already Marketed	Total
Priority review								
Discovered by PSRI (no.)	44	1	17	3	0	1†	0	66
All FDA approvals (no.)	209	6	99	20	14	0	0	348
Rate of PSRI discovery (%)	21.1	16.7	17.2	15.0	0	NA	NA	19.0
Standard review								
Discovered by PSRI (no.)	20	0	36	6	7	8	0	77
All FDA approvals (no.)	274	33	631	96	137	10	12	1193
Rate of PSRI discovery (%)	7.3	0	5.7	6.3	5.1	80.0	0	6.5
All approvals								
Discovered by PSRI (no.)	64	1	53	9	7	9	0	143
All FDA approvals (no.)	483	39	730	116	151	10	12	1541
Rate of PSRI discovery (%)	13.3	2.6	7.3	7.8	4.6	90.0	0	9.3

* NA denotes not applicable, and PSRI public-sector research institution.

† The second new-drug application approved for Pfizer's Sutent, in 2006, was classified as type 6 (new indication) and given a priority review. However, the totals supplied by the FDA showed no priority reviews for new-indication applications in 2006 or any other year.

One could argue that transfer of the knowledge and IP created by public sector research institutes with public sector investment should not be a basis for high-priced products. In other words, should the public have to pay twice? It seems only fair that if a product is developed with substantial public funding the price charged to the public should reflect that fact. Government investment into medical R&D is substantial, especially in the US. Of course, the levels of such investment differ tremendously per country.

New drug development is costly. And the current innovation system is in need of change to become less costly and more responsive to health needs, especially those of neglected populations. Models are needed that lead to sharing the results of research, that ensure transparency of clinical trial results to enable independent assessment of the value of a product and, perhaps most importantly, that include new models of financing drug development.

A global approach to the sharing of R&D costs to deal with the free rider issues, where one country benefits from the investment of another without making a contribution will, therefore, be required. Such an international approach should be coupled with measures to ensure equitable access to those innovations. One proposal is to delink the cost of the R&D from the price of the product and develop new ways to share the burden of innovation cost internationally. Some have proposed an international agreement on medical R&D to achieve the objectives of financing for innovation *and* access to those innovations.⁴⁵ A joint WTO, WIPO, WHO study describes delinkage as follows:

*One important concept that evolved from this discussion is the concept of delinking price of the final product from the costs of R&D. This concept is based on the fact that patents allow developers to recoup the costs and make profits by charging a price in excess of the costs of production. This way of financing R&D is viewed as constituting a barrier to access to medicines in countries where populations pay out of their own pockets for medicines and thus cannot afford to pay high prices. The principle of delinking is based on the premise that costs and risks associated with R&D should be rewarded, and incentives for R&D provided, other than through the price of the product.*⁴⁶

If, for example, the research and development cost of new cancer drugs would not have to be recouped through high drug prices in a few countries those medicines would cost less and would be more widely available.

3 CANCER AND CANCER MEDICINE PRICING

Is this going to have a big effect on our business model? No, because we did not develop this product for the Indian market, let's be honest. We developed this product for Western patients who can afford this product, quite honestly. It is an expensive product, being an oncology product.

Bayer CEO Marijn Dekkers responding to the Indian compulsory license for sorafenib (Nexavar) at the *Financial Times* conference 'Buffering the Pharma Brand: Restoring Reputation, Rebuilding Trust.'
3 December 2013.

Cancer is not one disease but refers to a large number of diseases. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then spread to other organs. Cancer is a leading cause of death worldwide and accounted for 8.2 million deaths in 2012. About 30 percent of cancer deaths are due to the five leading risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use, alcohol use. Sixty-five percent of all cancer deaths occur in developing countries. According to WHO, the number of global cancer deaths is projected to increase by 45 percent from 2007 to 2030 (from 7.9 million to 11.5 million deaths), influenced in part by an increasing and aging global population. The estimated rise takes into account expected slight declines in death rates for some cancers in high-income countries. New cases of cancer are estimated to jump from 11.3 million in 2007 to 22 million in 2035. Of all cancers, 30–40 percent are preventable.⁴⁷

While death rates from cancer in wealthy countries are declining because of early diagnosis and the availability of treatment, this is not the case in the low- and middle-income countries where effective treatment is often unavailable.

In India, as is generally true of other low- and middle-income countries, cancer is also on the rise. The Indian National Cancer Registry Program (NCRP) supports a number of local cancer registries throughout India, almost all in cities. The NCRP estimated the number of cancers in India at 946,172 in 2008, based on data from 2005–2006, rising to 1,148,758 in 2020.⁴⁸

Much of this rise is because the population is aging, since almost all cancers occur more frequently at older ages. In addition some risk factors associated with cancer are on the rise. The 2011 census showed that 4.8 percent of the population was over 65 years of age. That is not a high percentage by world standards. However, the rate of older people in India has risen steadily since 1941, beginning with about 5 percent of the population over the age of 60, and rising to 7.7 percent by 2001.⁴⁹ The incidence of certain cancers is rising. For example a study projecting the number of cancer cases in India estimated that:⁵⁰

- breast cancer incidence will rise from 90,659 in 2010 to 123,634 (in females) in 2020;
- lymphoid leukaemia will increase from 15,802 cases in 2010 in males and females to 18,449 cases in 2020;
- myeloid leukaemia will increase from 24,497 cases in 2010 in males and females to 34,701 in 2020;

- the total number of all cancer cases in 2010 was 979,786 and is estimated to rise to 1,148,757 in 2020;
- cervical and breast cancer is projected to account for 20 percent of all cancer cases in India.

Cancer care in India

There are specialized cancer centres spread throughout India, especially in major cities such as New Delhi and Mumbai. These are thought to provide high quality care. The problem is that the majority of patients present to a cancer treatment centre in the late stages of the disease when cure is usually unlikely. For example, only 9 percent of women with breast cancer present early when treatment is usually successful.⁵¹ In a chapter on cancer, a national report on the burden of disease states that treatment results for cancer are 20 percent lower than those in other countries.⁵²

Prevention and screening are not strategies commonly used in India. As in other health areas, the public health activities concerning cancer are weak.⁵³ Indian cancer specialists know that concentrating on treatment without attending to prevention amounts to a poor strategy. However, to take the example of breast cancer, mammography screening is 'not applicable' in India. Once a year clinical breast examination should be feasible, but is not being done at present.^{54, 55}

Access to cancer treatment in India also suffers from weaknesses of national health policy and lack of public health laws.⁵⁶ Insufficient financing, as well as inadequate human resources and facilities have resulted in a concentration of services in urban areas. Many people must borrow money to access treatment. A large, unknown number of people in rural areas cannot get treatment at all.⁵⁷

Cancer drugs are often very highly priced. These drugs, as in the case of other drugs, are mostly paid for out-of-pocket. The National List of Essential Medicines of India contains 348 drugs and includes the cancer drugs listed in the WHO Model List of Essential Medicines (see section 4.4) and some that are not on the WHO Model List. For example, imatinib is on the National List of Essential Medicines in India.⁵⁸

The price of newer generations of cancer medicines poses an important challenge for India, a country seeking to expand universal cancer care for its population. It may explain the requests for compulsory licenses for three cancer drugs (trastuzumab, ixabepilone, and dasatinib) made to the Department of Industrial Policy and Promotion (DIPP) by the Ministry of Health.

Prices of selected essential cancer drugs in low- and middle-income countries

The report of the 'Global Task Force on Expanded Access to Cancer Care and Control' provides estimated drug therapy costs for a selection of chemotherapy and hormone therapy in low- and middle-income countries. See Table 3.

One can draw the following conclusions from this table:

- some cancer treatments can be provided at relatively low cost;
- prices of single-source products are significantly higher than multi-source products and not affordable for low- and middle-income countries;
- prices of the same treatments can differ widely.

The table shows that the lowest/highest price ratio for certain products varies from 1 to 33. While patents can explain the high prices of 2 out of the 15 products in the table, patents are not the reason for the price discrepancies seen for the same product. For example tamoxifen, which has the highest low/high price ratio is not patented anymore and available from multiple sources. These discrepancies indicate that greater price transparency can help procurement officials to make better choices. Officials can use the global market pricing information to select the best value for money and increase access to treatment for more eligible patients.

Table 3 – Indicative chemotherapy and hormone therapy costs for selected essential medicines for cancer in low- and middle-income countries

Agent (a)	Patent (y/n)	WHO	EML	Indicative cost per treatment (\$)			High/low ratio
		adult	child	low	medium	high	
Anastrozole	n			172	432	2,086	12
Asparaginase	n	x	x	233	455	729	3
Carboplatin	n	x		380	480	2,333	6
Cisplatin	n			38	60	480	13
Cyclophosphamide	n	x	x	44	111	240	5
Dacarbazine	n	x		382	772	1,159	3
Doxorubicin	n	x	x	199	238	1,140	6
Imatinib	y			28,295	37,259	46,224	2
Mercaptopurine	n	x	x	613	1,596	2,877	5
Methotrexate	n	x	x	99	117	135	1
Paclitaxel	n	x		658	1,609	12,250	19
Rituximab	y			16,031	19,125	21,186	1
Tamoxifen	n	x		16	206	548	33
Vinblastine	n	x		114	218	461	4
Vincristine	n	x	x	26	57	71	3

(a)Based on Essential Package of Cancer Services and Drugs for Low- and Middle-Income Countries. October 28, 2011. Page 157. http://gtfcc.harvard.edu/fs/docs/icb.topic1063570.files/ccd_report_111027.pdf

Estimated costs for anastrozole, imatinib, and tamoxifen are per year; costs can vary depending on length of treatment course; each chemotherapeutic agent is part of a multi-regimen treatment protocol used for the specific kind of malignancy – so total treatment costs for specific cancers will vary.

Pricing data in this table are indicative of buyers' prices, usually government agency international bidding, or tender, prices from public sources and are from the MSH Drug Price Indicator Guide which uses reputable suppliers who meet quality standards.

Cases of specific cancer drugs

In this section we will describe some of the cancer medications that have been the subject of controversy, mostly because of high pricing. We have selected proven effective treatments and a mix of older and more recent products: dasatinib, docetaxel, erlotinib, imatinib, letrozole and trastuzumab. Of these, only imatinib is included in the National List of Essential Medicines of India. Three of the six medicines, docetaxel, letrozole, and trastuzumab are medicines used in the treatment of breast cancer. Breast cancer is the fastest growing cancer in India, and worldwide the most common cancer in women.

Table 4 below shows the average generic and originator price per tablet or injection for dasatinib, docetaxel, erlotinib, imatinib, letrozole, and trastuzumab in India, South Africa, the UK, and the US. The difference between generic and originator prices is significant and shows that access to generic supply is key to lowering the cost of treatment. However, within single-source products, huge price differences can also be seen. For example, the average price for one trastuzumab injection in South Africa is \$2,115 while the US average retail price is \$631 and the average UK hospital price is \$317. These price differences indicate that South Africa could create savings through price negotiations and better procurement.

Table 4 – Average price of six cancer drugs in four countries

Average trade price in US\$ per unit	DASATINI B	DOCETAX EL	ERLOTINI B	IMATINI B	LETROZO LE	TRASTUZUM AB
	Per Tablet	Per Injection	Per Tablet	Per Tablet	Per Tablet	Per Injection
Generic						
India (total sales)		114.41	11.76	2.65	0.40	941.58
S- Africa (total sales)		241.41		12.46	2.76	
UK hospital	79.06	496.18			0.40	
UK retail	79.06	825.08			0.72	
US clinic	162.39	305.73			0.18	
Innovat or						
India		133.85				
S-Africa	48.82	245.74	44.04	36.09	4.80	2,115.61
UK hospital		602.26	57.40	43.81	4.97	317.73
UK retail		720.19	57.40	43.81	4.97	631.25
US clinic		587.49	107.66	24.11	10.10	2,907.49

Source: IMS 2013.

Trastuzumab - Roche (breast cancer)

Trastuzumab is a biotechnology product (monoclonal antibody) indicated for the treatment of specific types of breast cancer. The US approved indications for trastuzumab are:⁵⁹

- HER2-overexpressing Metastatic Gastric or Gastroesophageal (GE) Junction Adenocarcinoma – FDA approval in 2010.
- HER2-overexpressing Breast Cancer – FDA approval in 2006.

Trastuzumab is either prescribed as a monotherapy or as a combined/adjuvant therapy with other chemotherapeutic agents (cisplatin or docetaxel or paclitaxel).

Trastuzumab was developed and patented by Genentech and is currently marketed by Roche as Herceptin. Roche acquired Genentech in 2009⁶⁰ and holds the patent in certain countries. The patent expiry date of the base compound is 2014. This patent was not granted in India because the product was developed before 1995 when India did not grant patents for pharmaceutical products. In 2007, a secondary patent was granted in India to Genentech (the original developer, later acquired by Roche) on a composition of the drug. This patent was valid until 2019.

However, Roche has relinquished its patent for trastuzumab in India. Roche did this after the Kolkata patent office had revoked patents related to trastuzumab.^{61,62}

Roche has entered into an agreement with the Indian generic manufacturer Emcure Pharmaceuticals Ltd. for lower priced (31 percent reduction) supply of trastuzumab.⁶³ Technically Emcure's product is not a biosimilar because it simply repackages the product produced by Roche. In January 2014, a Bangalore-based biotech company in partnership with US generic drug maker Mylan announced plans for the marketing of a trastuzumab biosimilar priced at \$933 per vial which is 25 percent lower than the Roche product in India.^{64,65} Roche has attempted to challenge the marketing of biosimilar trastuzumab quoting misrepresentation as 'biosimilar Trastuzumab' and 'biosimilar version of Herceptin' without following the 'due process in accordance with the guidelines for similar biologics' for getting approvals in India.⁶⁶

On 26 November Biocon and Mylan received marketing authorization in India for their biosimilar trastuzumab products which they each market under separate brand names.⁶⁷

Trastuzumab is not on the WHO Model List of Essential Medicines (EML). In November 2012, Knowledge Ecology International, the University of California, San Francisco, Universities Allied for Essential Medicines (UAEM) & Young Professionals Chronic Disease Network (YP-CDN) submitted trastuzumab for inclusion in the WHO Model List of Essential Medicines. In their application they point out that one possible supplier of trastuzumab suggested the drug could be manufactured for \$31 per gram, or \$242 per year, roughly 1 percent of the lowest Roche price. The current Roche prices range from \$3,000 to \$9,000 per gram (1 gram of gold costs \$42 – 4 November 2013).⁶⁸

The WHO Expert Committee did not accept the proposal for inclusion of

trastuzumab but acknowledged that an urgent review of the entire section of cytotoxic medicines on the EML is called for. The Expert Committee considered the applications in detail and noted the high quality evidence showing relevant clinical benefits in support of both imatinib and trastuzumab but deferred the final specifications of the medicines and their inclusion until the review of the section of cytotoxics is completed.⁶⁹ The review by WHO of the section of cancer medications of the EML is due mid-2014.

Table 5 – Price of trastuzumab in \$ for a one-year course⁷⁰

This table provides prices as quoted in different sources for trastuzumab.

Country	Originator	Generic
US	49,000	
UK	25,000 (2)	
India	16,392 (4) 28,182 (6)	14,000 (3) 24,000 (6) (Emcure) 11,600 (5) (Biocon) ⁷¹
China	54,000 (1)	
South Africa	46,748 (6)	

(1) <http://www.ispor.org/consortiums/asia/ViH/An-Economic-Evaluation-of-Adjuvant-Trastuzumab-Therapy.pdf>

(2) NICE

(3) http://articles.economictimes.indiatimes.com/2013-02-01/news/36684537_1_cancer-drugs-roche-herceptin

(4) <http://www.fiercepharma.com/story/indias-biocon-promises-herceptin-biosim-launch-fiscal-year-end/2013-08-21>

(5) <http://www.bloomberg.com/news/2014-01-20/roche-herceptin-copy-s-price-still-out-of-reach-in-india.html>

(6) KEI trastuzumab_price_survey. Available here:

<https://docs.google.com/spreadsheets/pub?key=0AmvILxGkIHUdDJTRkx0anBKN0o4Z2FkLWVmbFlvMGc&gid=2>

Box 2 – Breast cancer

Breast cancer is a cancer that forms in the tissues of the breast. Breast cancer occurs in both men and women, although male breast cancer is rare. In 2013, an estimated 232,340 women were diagnosed as having breast cancer in the United States, and an estimated 39,620 women died from breast cancer. The age-adjusted incidence rate of breast cancer in the United States is 123.8 cases per 100,000 women. This may be contrasted with the age-adjusted incidence rate of 22.8 per 100,000 in India in 2006, projected to be the same in 2015.⁷² In terms of burden of disease (Disability-Adjusted Life Years - DALYs), the US had 678.42 DALYs in 2010, while India had 232.98. Breast cancer is the most common cancer in women in India.⁷³

A number of factors have been found to be associated with breast cancer, including family history, nulliparity (no pregnancies), early menarche (menstruation), advanced age, and personal history. Of all women with breast cancer, 5–10 percent are found to have the BRC1 or BRC2 gene, and women with one of those genes have a 40–85 percent lifetime chance of developing breast cancer. Breast cancer is also associated with certain exposures, especially synthetic oestrogen (DES).

Breast cancer can be suspected when a lump is found in the breast, when the breast has changed sizes, when there is discoloration of the skin of the

breast, and other signs. Diagnosis begins with a professional medical history and physical examination, including breast examination. Further diagnostic tests include x-ray mammography (which is also used as a screening tool for early identification and diagnosis of breast cancer), ultrasound examination, magnetic resonance imaging (MRI) examination, and blood chemistry examination. If breast cancer is suspected from these examinations, breast biopsy is carried out. In addition to microscopic examination of the tissue, tests that can be carried out including oestrogen and progesterone receptor tests, human epidermal growth factor type 2 receptor (HER2/neu) test, and multigene tests.

For the purposes of this project, the HER2/neu test is particularly pertinent, because it can indicate a cancer that will grow faster and spread faster than other cancers. In such cases, the drug trastuzumab is indicated in primary treatment. Approximately 25 percent of cancers in the United States overexpress HER2/neu and are thus candidates for treatment with trastuzumab.

The treatment of breast cancer depends on the stage of the cancer. Simply speaking, breast cancer is classified into 4 groups, beginning with very small cancers in group 1, larger cancers in groups 2 and 3, and cancers with local extension of the cancer or spread through the body (or inflammatory cancers) in group 4. Spread may be determined by such methods as lymph node biopsy, chest x-ray, computed tomography (CT) scan, bone scan, or positron emission tomography (PET) scan. The treatment and prognosis are closely related to the stage of the cancer.

Treatment for breast cancer in all stages up to stage 4 always involves surgery. In stage 4, that is, with cancer that has spread beyond the breast, surgery is of limited benefit. In such cases, chemotherapy and/or hormone therapy are routinely used. Trastuzumab is a commonly used type of chemotherapy in this situation. Radiation therapy is also sometimes used with stage 4 cancers. Treatment of stage 4 is palliative in intent. The purpose is to improve quality of life, and, perhaps, to prolong life. Median survival is 18–24 months, although some patients live considerably longer.

For patients with stage 4 metastatic cancer overexpressing HER2/neu, a chemotherapeutic agent plus trastuzumab is recommended for treatment by the US National Cancer Institute.

Letrozole (Femara)– Novartis (breast cancer)

Letrozole is approved by the United States Food and Drug Administration (FDA) for the treatment of local or metastatic breast cancer that is hormone receptor positive or has an unknown receptor status in postmenopausal women. Letrozole is not on the WHO Model List of Essential Medicines. Letrozole is marketed by Novartis under the brand name Femara. The product is not patented in India, because it dates back to pre-1995, a period in which India did not grant product patents. In the US the patent expired in 2010. CIMS lists 33 producers offering the product. The price difference between

the originator and the lowest generic price in India is noteworthy with a high/low price ratio of 41.

Table 6 – Retail price of letrozole in India (per 2.5mg tablet)

Brand Name of letrozole	Company	Price Indian rupees (Rs.) (\$ exc. rate 11.11.13)
Femara	Novartis	248.20 (4.50)
Oreta	Dr Reddy's	37.80 (0.68)
Letromac	Maclead's	33.80 (0.61)
Anolet	Zvizera	27.00 (0.49)
Fempro	Cipla	6.00 (0.10)

Source: CIMS.COM

In 2008, Thailand issued compulsory licenses for four anti-cancer drugs, including letrozole, to allow the use and importation of generic versions from India where those products were not patented and from where they could be exported without further legal requirement. The justification for the decision was the high price charged by Novartis. The price of one tablet of 2.5mg of Novartis's letrozole was 230 Baht (\$ 7.35), while the price of the generics was 6–7 Baht (\$0.19 –0.22), representing a price differential of 30.⁷⁴

Imatinib mesylate (Gleevec) – Novartis (CML)

Imatinib mesylate is the drug of choice to treat chronic myeloid leukaemia and is marketed by Novartis as 'Glivec' or 'Gleevec'.⁷⁵ The invention of the original Gleevec compound dates back to 1993, the pre-1995 period when India did not have a product patent system.⁷⁶ Nor was it possible to make a mailbox application because the mailbox system was not established until 1995, according to WTO requirements. In 1998, Novartis did submit a mailbox patent application for the new form of imatinib mesylate.

It was this patent application for Imatinib that became subject to fierce battles over its patentability in India. Natco Pharma Ltd., an Indian drug firm that produced a generic version of the product, and the Cancer Patients Aid Association (CPAA) opposed the grant of the patent.

In 2006 the Indian Patent Office rejected a patent application by Novartis for the beta crystalline form of imatinib mesylate. Novartis appealed the decision of the Indian Patent Office. After a seven-year battle in the Indian courts, the Supreme Court of India on 1 April 2013 confirmed that the patent application failed to meet the requirements for patentability under Indian law. Public health advocates the world over closely monitored the court case because of its potential effect on the supply of affordable generic medicines originating in India.

The patent application for the beta crystalline form of imatinib mesylate was rejected because it was not considered innovative. In other words it concerned a modification of a known molecule. Indian patent law (section 3(d)) explicitly requires that patents only be granted for compounds that are

truly new and innovative. For new forms of known compounds, Indian law requires patent applicants to prove significantly improved efficacy to achieve eligibility for a patent. India introduced this requirement to prevent the practice of continually extending or 'evergreening' of medicines' patents by seeking patents for minor alterations to the original molecule or known compounds. The Supreme Court clarified that this requirement of improved efficacy refers to therapeutic efficacy. Thus, the Supreme Court ruled that the Novartis application for a patent for imatinib mesylate did not meet the requirement of section 3(d).

Box 3 – Section 3(d) Indian Patents Act

The text of Section 3(d) of the Indian Patents Act reads as follows:
'the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.'

In practice this means that the Indian patent law explicitly requires that patents only be granted for compounds that are truly new and innovative. For new forms of known compounds, Indian law requires patent applicants to prove significantly improved efficacy to achieve eligibility for a patent. Section 3(d) was designed to prevent the so-called 'evergreening' of patents, which refers to a business strategy to extend market exclusivity of a product by seeking patent protection for changes to that product. One example is seeking a patent on a combination of 2 known medicines. Evergreening strategies aim to delay the entry of generic versions of the product.

Indian law does not allow such patents. Section 3(d) is not in conflict with India's obligations under the TRIPS Agreement. The TRIPS Agreement obliges countries to provide patents but allows flexibility in determining national patentability criteria. This also explains why certain patents are granted in one country while they are rejected in another.

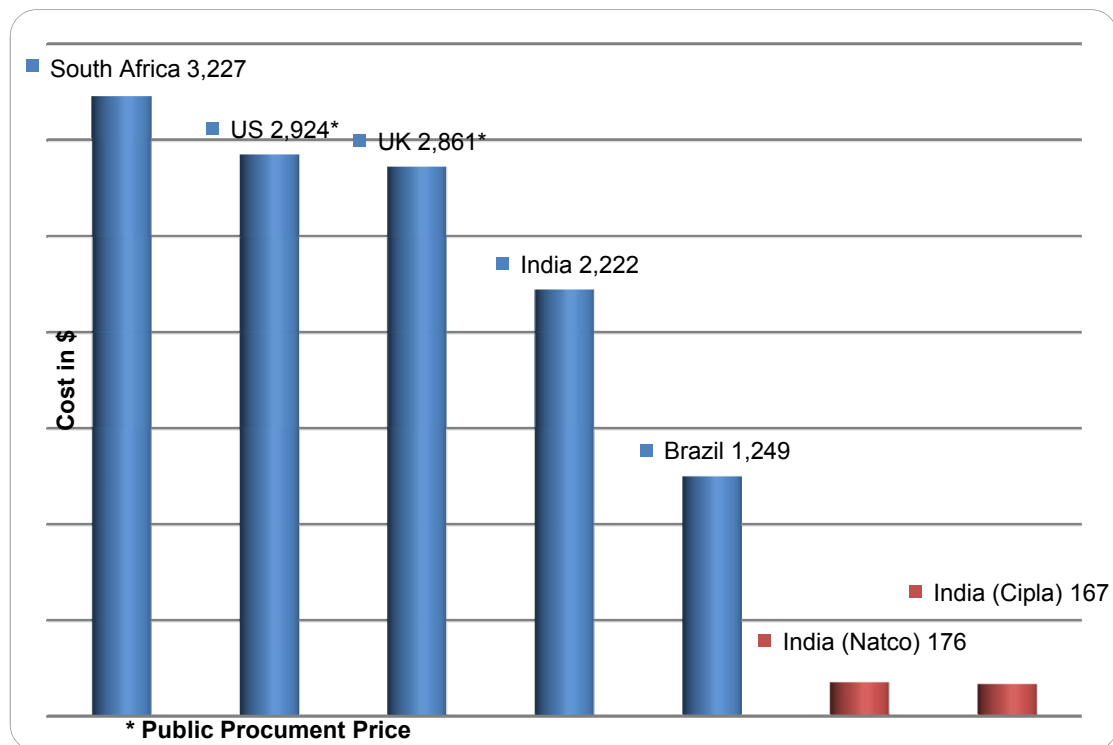
Throughout the seven-year court battle the public health community around the world paid close attention for at least two reasons:

- the expanded supply of low-cost generic imatinib mesylate was at stake – with the Indian generic price at \$170 versus \$2,200 per month from Novartis; and
- the effectiveness of section 3(d) was at stake. Section 3(d) has been the basis of successful patent grant oppositions by patient groups and other civil society organizations. For example, this provision helped to increase generic supply of low-cost antiretroviral medicines to treat HIV/AIDS in the developing world.

Graph 1 below gives the price of imatinib per patient per month in various countries showing the steep discounts that can be obtained when there are no patent barriers to generic drug makers entering the market. Imatinib is on the National List of Essential Medicines of India.

In 2008, Thailand issued a compulsory license for imatinib, price being the main reason.⁷⁷ The price of a 100mg tablet of the originator brand costs 917 Baht (\$29.30), while the generic version costs 50–70 Baht (\$1.59–2.23), representing a price differential of almost 20 times the amount for a patented medicine than its generic equivalent. A government assessment of the effect of the compulsory license (CL) concluded that by 2009 the availability of imatinib in the Thai health care system had led to 2435 quality-adjusted life years (QALYs) gained.

Graph 1 – Cost of imatinib brand Gleevec (blue bars) and cost of generic imatinib per patient per month (red bars)



Source: MSF-India 2013

Box 4 – Leukaemia

Leukaemia is a cancer of the blood-forming organs, such as the bone marrow, that causes large numbers of abnormal cells to enter the circulation of the blood. Leukaemia is named for the type of affected cell, either the lymphoid cell or the myeloid cell. The estimated number of new cases of leukaemia in the United States in 2013 was 48,510. The estimated number of deaths was 20,720. In terms of burden of disease, the US had 165.35 DALYs per 100,000 in 2010. India had 102.56 DALYs per 100,000. Leukaemia is the leading cancer of children.

Leukaemia is grouped by how quickly the disease develops and worsens. Chronic leukaemia develops slowly and the blood cells behave somewhat normally. Symptoms are mild at first and may be slow to develop. Acute leukaemia develops more quickly and the cells do not do their normal work.

Acute leukaemia usually worsens quickly. Leukaemia causes many symptoms. Some symptoms that may be seen include weakness and tiredness, fever, easy bruising, shortness of breath, weight loss, pain in the bones and joints, swollen lymph nodes, and frequent infection. Diagnosis is done by medical examination and lab testing, including blood count and differential, blood chemistry, tests of blood coagulation, and active screen for infection. Treatment is primarily by chemotherapy.

Acute Lymphocytic (Lymphoblastic) Leukaemia (ALL)

This type of leukaemia affects the lymphoid cells. It is the most frequent cause of leukaemia in children, but also affects adults. There are about 5,000 cases a year in the United States. Among children with ALL in the United States, more than 95 percent attain remission. Approximately 80 percent of children from age 1-18 will have a prolonged remission without symptoms. Treatment is by chemotherapy agents, such as vincristine and corticosteroids. This treatment is difficult and must be carried out in a specialized medical centre where supportive care, including transfusions, is possible.

Successful treatment of adults with ALL also relies on chemotherapy. It is important to treat or prevent 'sanctuary-site disease', especially in the central nervous system. Younger patients have a better prognosis, and signs of central nervous system involvement indicate a poor prognosis.

Chronic Myelogenous (Myeloid) Leukaemia

This cancer is of the myeloid cells and is seen predominantly in adults. There are an estimated 5920 cases of CML in the United States in 2013 and 620 deaths. The most common finding during diagnosis of CML is an enlarged spleen. Laboratory diagnosis is usually easily carried out because of typical cells. The median age of CML patients is about 67 years. Longevity was about four to six years, but it is improving with the availability of newer agents. For information about CML in India see Chapter 3.

Dasatinib (Sprycel) – Bristol-Myers Squibb (CML)

Dasatinib is sold as Sprycel by Bristol-Myers Squibb. Dasatinib received USFDA indication for Chronic Phase Philadelphia chromosome-positive Chronic Myelogenous Leukaemia (CP-CML) in 2010.

Other indications are: Chronic Phase (CP) Chronic Myelogenous Leukaemia (CML) with resistance or intolerance to prior therapy (FDA approved in 2007) and Chronic Myelogenous Leukaemia (CML) and Philadelphia chromosome-positive Acute Lymphoblastic Leukaemia (ALL) with resistance or intolerance to prior therapy (FDA approved in 2006).⁷⁸

According to La Revue Prescrire (LRP), based on currently available evidence, imatinib is a better choice for 1st line treatment. LRP considers dasatinib possibly helpful in CML patients not responding to other treatments e.g. imatinib. Long-term data on survival with dasatinib versus imatinib is currently lacking.⁷⁹

The three US patents on dasatinib are held by BMS and will all expire in 2020.⁸⁰

According to Knowledge Ecology International, based upon the data publicly available regarding clinical trials, it is estimated that BMS spent between \$6.5m and \$26m on clinical trials related to the FDA approval of the BMS version of dasatinib, for the indications ALL and CML. US-government funding for clinical trials for treatment of leukaemia was substantial. See Table 7.⁸¹

Table 7 – Clinical trials sponsorship

Condition	All trials	Industry-funded trials	NIH funded	(%) Industry	(%) NIH
ALL	90	55	29	61	32
Leukaemia	38	25	12	66	32
Leukaemia/CML	18	17	1	94	6
Leukaemia/ALL	16	10	5	63	32

Source: *clinicaltrials.gov* July 3 2008. Compiled by KEI.

BMS applied for and obtained orphan drug status for dasatinib in the US and the EU, but not in Japan. Orphan drug status can be obtained for the development of a treatment for diseases with a relatively small patient base. Orphan drug status for a product means that the company can benefit from tax breaks for clinical trial expenses, additional marketing exclusivity, lower registration fees and/or direct grants.

When queried about the price of Sprycel, BMS responded as follows:

We price our medicines based on the cost to develop them, the scientific innovation they represent, and the value they deliver to patients and physicians. The price of SPRYCEL reflects the company's robust research and development program for this drug moving forward and competitive market pressures that affect our pricing considerations.
(Source: email from BMS to KEI, 22 July 2008)

In January 2013, following an expert committee's recommendation, the Indian Minister of Health recommended dasatinib for compulsory licensing to the Department of industrial policy and promotion (DIPP). DIPP is still examining the request by the MoH and a decision is pending.⁸²

Separately, the generic company BDR Pharmaceuticals also applied for a CL to be able to produce and market dasatinib.

BDR said its generic dasatinib would be available to patients at Rs. 135 (\$2.2) per tablet. BMS' estimated comparable price is about Rs. 2,761 (\$43.57). BDR offered to pay a royalty and make the product available free to a certain percentage of patients. This request for a compulsory license, however, was rejected on procedural grounds – failure to meaningfully engage in obtaining a voluntary license from the patent owner – on 29 October 2013.⁸³ BDR and BMS are also engaged in litigation over dasatinib before the Delhi High Court.

Mims India lists 2 suppliers of dasatinib: Bristol-Myers Squibb and Natco Pharma Ltd. that make a generic version of dasatinib. The price difference is telling.

BMS and Natco have been engaged in a patent infringement battle over dasatinib and a Delhi High Court injunction in June 2012 prohibited Natco from continuing to sell the product.⁸⁴ At least 2,500 patients were on treatment using Natco's generic dasatinib, until it was withdrawn following the Delhi High Court order in June 2012.

Table 8 – Retail price Dasatinib 50mg tablet

Brand name	Company	Price per tablet 50mg (\$)
Dasanat	Natco Pharma Ltd.	2.33
Sprycel	Bristol-Myers Squibb	52.20

Source: Mims.com (2013)

Docetaxel (Taxotere) – Sanofi-Aventis (breast cancer)

Docetaxel is used mainly for the treatment of breast, ovarian, prostate, and non-small cell lung cancer. The originator brand is Taxotere and it is sold by Sanofi-Aventis who acquired it after the merger with Rhône-Poulenc Rorer (RPR). RPR developed docetaxel following the discoveries of researchers at CNRS working on improvements to the production of Taxol.

Box 5 – The case of Taxol

Taxol or paclitaxel is isolated from the bark of the Pacific yew tree (*Taxusbrevifolia*) and was discovered in 1967 by a US National Cancer Institute. Taxol was developed under a 1991 cooperative research and development agreement between NIH and BMS. The FDA approved Taxol in 1992.

The high price of the product and concerns about the technology transfer of government funding innovations to the private sector lead to an investigation of the NIH–BMS agreement by the General Accounting Office which concluded that: *NIH made substantial investments in research related to Taxol, but its financial benefits from the collaboration with BMS have not been great in comparison to BMS's revenue from the drug.*⁸⁵ Some key findings leading to this conclusion are below.

- The total R&D investment towards the development of Taxol by NIH had been \$484m.
- BMS's sales of Taxol between 1993 and 2002 were valued at \$9bn.
- The government, mainly through Medicare, contributed significantly to payments for Taxol: \$687m between 1994 and 1999.
- Royalties to NIH were 0.5 percent and netted the government \$35m.
- The 1991 agreement between NIH and BMS included a fair pricing requirement but it did not require that evidence be presented to assure that Taxol was reasonably priced.

Taxol was the precursor of docetaxel and also a result of a Cooperative

Research and Development Agreement (CRADA) between a company and NIH. Docetaxel (Taxotere) was approved by the FDA in 1996.

Docetaxel was protected by US and European patents which were owned by Sanofi-Aventis. The European patent expired in 2010. Docetaxel continues to be an important anti-cancer medication. It is part of the WHO EML and the Indian national EML.

In 2007, Thailand announced compulsory licence plans for docetaxel to be able to access lower priced versions of the product for use in its healthcare system.⁸⁶ The Indian company Venus won an open bid to supply the Thai healthcare system.⁸⁷

Today there are several generic versions available on the world market. A full treatment cost varies from \$42 to \$346, making the treatment affordable for use in health systems in low- and middle-income countries. India has 26 different producers offering docetaxel.⁸⁸

4 LESSONS FROM HIV AND PRICING OF ARVS

The myths surrounding efforts to expand cancer care—not a problem, not affordable, not possible, will divert resources from higher priorities—once held back progress in AIDS. Yet we have seen remarkable success expanding access to HIV & AIDS services. We can do the same for cancer. Closing the cancer divide would be a broad investment in the health, as well as the economic and social well-being, of people throughout the world.

Dr Jonathan Quick, President and Chief Executive Officer of Management Sciences for Health

In the late 1990s the pricing challenges of HIV medicines in developing countries were comparable to the pricing challenges we see today with cancer drugs. Highly active antiretroviral (ARV) treatment was available in wealthy countries and had changed AIDS from a death sentence into a manageable chronic disease. But the drugs (ARVs) were available only from originator companies, who controlled the patents. They produced small quantities carrying paralysing price tags – \$10,000 to \$15,000 per person per year. However, in the last decade the price of HIV medicines has dropped dramatically with changes up to 99 percent and 10 million people living with HIV in low- and middle-income countries today have access to treatment. The drop in price of medicines was crucial in the drive to scale up treatment for people living with HIV. What are the lessons we can draw from ARV pricing for cancer treatment? And what are the differences?

Market for cancer drugs

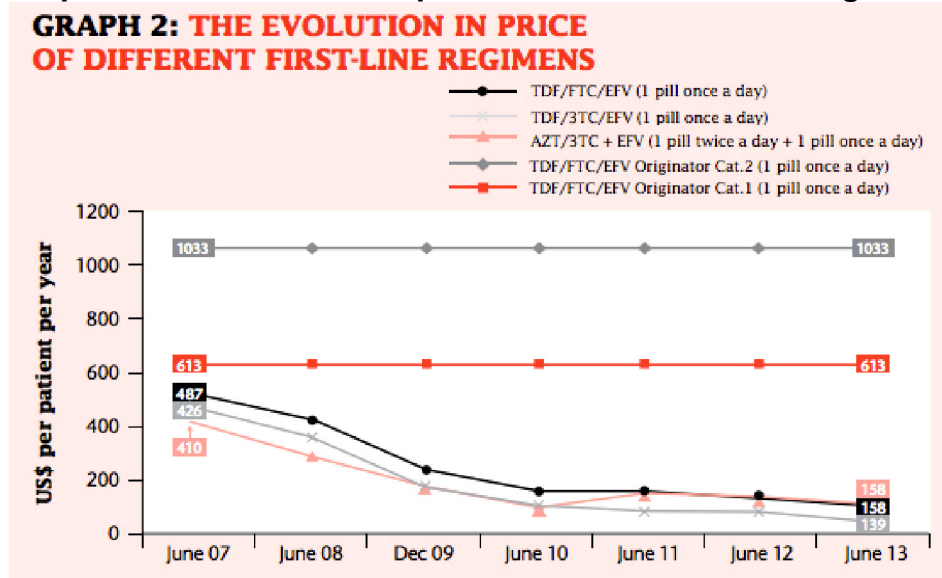
Cancer is different from HIV. Cancer is not one disease. There are many different forms of cancer and each form of cancer and stage of the disease require a different intervention. Most cancers, as part of the primary treatment, require surgery and or radiation. There are only a few cancers that can be successfully treated only with chemotherapy (medicines). This characteristic makes cancer different from HIV, which is an infectious disease that can be successfully managed solely with medicines that people can take at home or in their communities.

It may also affect the potential market size. Part of what drove the drop in prices of HIV medicine was the size of the market and the global funding available to create this market. These market conditions do not as yet exist for cancer treatments in low-and middle-income countries.

Generic competition

Generic competition in the HIV market has been essential in bringing the price of antiretroviral medicines down dramatically. Prices of ARVs in the late 1990s were set globally by the originators and were around \$10,000 to \$15,000 per patient per year. Generic competition, mostly from companies in India, has since then brought the price down significantly. And prices continue to drop. The graph below shows reductions in the prices of the generic versions of the WHO recommended first line triple therapy, as against prices of the originator since 2007. The prices of the generic products of the triple combination (TDF/3TC/EFV) have fallen by 67 percent since 2007, while the originator price has remained the same since 2007.

Graph 2 – The evolution in price of different first line regimens



Source: MSF *Untangling the web of antiretroviral price reductions 16th edition*.

An analysis of price reduction strategies using the data sources on ARV procurement from the Global Fund and the WHO Global Price Reporting Mechanism (GPRM) shows the importance of generics and the failure of differential pricing schemes, which have not decreased the prices of branded ARVs to levels that can make these drugs universally accessible in low- and middle-income countries.⁸⁹

The effect of generic competition on the price of medicines is not confined to ARVs. The price comparisons of single-source versus multi-source cancer medication (see Chapter 3) indicate that generic production of cancer drugs can help bring prices down. However, the size of the developing world market for HIV drugs – that grew in response to political pressures – has certainly helped to attract manufacturers and to create the demand.

Small molecules vs. biologics – regulatory challenges.

Today's ARVs are so called small molecules. Inter-changeability with the originator product is necessary to obtain marketing authorization and WHO prequalification for generic versions. Inter-changeability of small-molecule products can be demonstrated with relatively simple bioequivalence studies. A generic manufacturer does not have to repeat full efficacy and safety clinical trials to do this. Regulatory requirements for biologics are different from requirements for small molecules. Increasingly, new cancer medications are called biotechnology products, meaning they are produced using living systems such as plant or animal cells, bacteria, viruses and yeast. A generic version of a biotechnology product is called a biosimilar product. The development of a biosimilar is different from a traditional small-molecule generic product because it is more complex and costly and thus requires significant investment by the generic producer.⁹⁰ Of the 52 new molecular entities with an FDA indication for cancer approved between 2000 and 2011, 15 (29 percent) were biotechnology products.

In the area of HIV the WHO prequalification programme of medicines plays a key role in providing regulatory pathways for generics. It has developed standards, opened the way for fixed-dose combinations, and provided national regulatory agencies with guidance on how to deal with fairly new medications in the field of HIV. Similar activity for biotechnology medicines, by WHO, does not exist at the moment. The regulatory standards for assessing and approving marketing of biosimilar products that exist in Canada, the EU, and the US differ from each other. There is a lack of clear regulatory pathways for biosimilar products in many countries and a lack of internationally agreed terminology and standards for assessing 'similarity'. In 2010, WHO published guidelines for the assessment of biosimilar medicines for national regulatory agencies (NRAs).⁹¹ There remains, however, a need for WHO to step up the development of product-specific standards for their assessments to deal with potential regulatory hurdles for biosimilar cancer products in developing countries, and for its donors to ensure that WHO is resourced to be able to do so.

Box 6 – Biosimilars and trade agreements

The US government is under pressure from its biotech/pharmaceutical industry to demand an exclusivity period of 12 years in the Trans Pacific Partnership (TPP) trade negotiations which would affect the availability of biosimilars.⁹² The US indeed tabled such a proposal at the TPP negotiating round in November 2013. It is important to monitor closely the biosimilars issue in the TPP negotiations because such negotiations in the past have often been a venue for the creation or expansion of non-patent-based exclusive rights for pharmaceuticals.⁹³

WHO Model List of Essential Medicines

In 2002, WHO included antiretroviral drugs in the WHO Model list of Essential Medicines (EML) for the first time. This was important because the EML is the basis for many national authorities to make their drug selections for their lists and it helps to stimulate uptake of the recommended treatments at national

level. The list also steers priorities in other medicine policy areas, such as the WHO Prequalification.

The WHO EML does not include cancer medicines on the core list. Cancer medications included in the WHO EML are on a so-called 'complementary list' and do not form part of the 'core list'. According to WHO, the complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed, or because of high cost.

The inclusion of ARVs in the EML was important in facilitating uptake of the recommended treatments at national level. The last WHO expert committee acknowledged that it should review the section on cancer medication.

Procurement issues and price transparency

It is not easy for procurement officers to have access to pricing information in order to make sound purchase decisions. This is different for HIV where organizations such as Médecins sans Frontières, UNICEF, and the Global Fund provide information about prices paid by them or their recipients. In response to this situation, Management Sciences for Health has published a list of 2010 cancer medicine prices, mostly based on products listed in the WHO's 17th edition of the EML.⁹⁴ This includes immunosuppressive medicines, cytotoxic and adjuvant medicines, hormones and anti-hormones, and medicines used in palliative care such as pain medication and psychotropic medicines. However, it seems obvious that since this is the only procurement tool available for authorities in low- and middle-income countries, more support is needed. An updated WHO EML section on anti-cancer drugs coupled with pricing information and procurement guidance would be a necessary first step.

Nevertheless, management of pharmaceuticals in HIV programmes provide important lessons for the procurement of medicines for NCDs, including anti-cancer medication. Hogerzeil et al. on behalf of the Lancet NCDs Action Group list the following actions:

- efficient selection and procurement and the use of generic medicines;
- increased mobilization of resources to meet the needs of people that currently have no treatment;
- the use of TRIPS flexibilities, such as compulsory licensing to lower the cost of patented medicines.

These recommendations are very much supported by the pricing information for cancer drugs and the wide range of prices available on the world market. Procurement of quality medicines at the best prices should be the standard procedure. Greater international price transparency will enhance financially sound procurement especially in low- and middle-income countries needing to make the largest public health impact with limited resources. If patents form a barrier to accessing lower-cost generic versions, the use of TRIPS flexibilities can help to overcome such barriers. Recourse to the use of TRIPS flexibilities is both legal and sometimes necessary when patents block national aspirations to develop cancer services.

Box 7 – Expanding access to affordable cancer care

The 'Global Task Force on Expanded Access to Cancer Care and Control' draws heavily on experiences in HIV when it lists the following elements of a pharmaceutical systems approach needed to increase access to affordable cancer care:⁹⁵

- international standard treatment guidelines (STGs);
- a list of essential medicines, vaccines, and health technologies for cancer;
- medicine price information and price reduction strategies;
- reliable national, regional, and global procurement mechanisms;
- effective quality assurance;
- engagement with manufacturers;
- action to address non-price barriers to palliation and pain control.

Political environment

HIV has a different political environment from cancer. A specialized UN agency for AIDS, UNAIDS, exists. And there are funding mechanisms as well as a very active civil society that includes organized groups of people living with HIV. The poorly controlled HIV epidemic was seen as a national security risk for the US early this century and was the subject of a study, by the US National Intelligence Council commissioned by the White House, which played an important role in the Bush administration's decision to create PEPFAR.⁹⁶

Cancer does not exist in a parallel political culture. The pharmaceutical industry and its supporters at the 2011 UN summit on NCDs lobbied hard to ensure that there was little attention to the high cost of medication to treat NCDs and instead steered the focus towards prevention rather than treatment of people who are ill. Sarah Boseley, who follows global health issues for *the Guardian* newspaper, commented:

*We are hearing much about the prevention of the 'lifestyle' (or non-communicable) diseases at the UN summit in New York, which is clearly a very good thing, but little about treatment for cancer, heart and lung disease and diabetes. Curiously, it was the other way round at the first UN high-level meeting on a health issue in 2001, when millions of people were dying from Aids.*⁹⁷

This is reminiscent of the earlier days of AIDS when the global health community advocated for prevention but not treatment. Political activism for HIV has turned this around and has been essential in many of the policy and funding developments that have made treatment possible on a large scale.

Such political activism does not yet exist for cancer or other non-communicable diseases, although the voices are becoming louder. A recent opinion piece in the newspaper *The Hindu* called for all essential medicines including anti-cancer drugs to be made available for free to all in need in India.⁹⁸ And the Indian Gleevec case received attention from activists the planet over and has spurred activism in South Africa for patent law reform.⁹⁹

Financing of HIV versus financing of cancer care

For HIV treatment there are international funding mechanisms entirely (PEPFAR) or almost entirely (Global Fund, UNITAID) devoted to scaling up treatment in low- and middle-income countries. There are no such funding mechanisms for cancer or other non-communicable diseases (NCDs). The MDGs, for example, do not have a target for NCDs. Some have argued that global health funding should become universal and move away from support to vertical programmes.¹⁰⁰ But in times of financial crisis a proposal to fund healthcare is bound to fall on deaf ears. However, the high price of some cancer medications should not be used as an excuse for inaction. Many cancers can be treated with cheaper generic medications that are currently available. In addition, the high price of some more recent cancer treatments do not reflect the cost to make them and increased funding for cancer care should go hand-in-hand with measures to bring the price of the newer essential cancer drugs down.

Conclusion

There are important lessons from HIV that are applicable for reducing the cost of cancer medications, in particular, costly patented products. However, the political, policy and financial forces that have driven global action on prevention and treatment of HIV for the last decade and a half do not as yet exist for NCDs such as cancer. The success of HIV treatment scale-up has shown it is possible to provide effective, sophisticated treatments even in the most resource-poor settings. The argument, therefore, that cancer treatment is complex should not be used as an excuse for inaction in the field of cancer.

5 PHARMACEUTICAL COMPANIES' ACCESS POLICIES FOR CANCER DRUGS IN LOW- AND MIDDLE-INCOME COUNTRIES

Developing country markets and in particular middle-income countries are increasingly important for the pharmaceutical industry because of market growth potential. In low- and middle-income countries there are huge unmet needs offering important sales opportunities. Pharmaceutical markets in high-income countries are, of course, important for the industry, but the growth of these markets has come to a halt or is slowing down. Table 9 shows that the double digit growth markets will be in Asia and Latin America in the next decade.¹⁰¹

Table 9 – Pharmaceutical market growth by region

Region	Market growth 2013 (%)	Market growth projections 2012–2017 (%)
North America	-2.7–0.3	0.7–3.7
Europe (EU + non EU)	-1.8–1.2	-0.4–2.6
Asia (including Indian Sub-continent) /Africa/ Australia	11.4–14.4	11.4–14.4
Japan	2.8–5.8	1.7–4.7
Latin America	9.0–12.0	10.0–13.0

Source: IMS Health Market Prognosis June 2013

Low- and middle-income countries often have a small but wealthy high-income population that is of interest to the industry because it can afford to pay for high-priced medicines. However, for companies to have a social license to operate in developing country markets they will have to develop strategies to serve the needs of the entire population, in the interests of public health.

This section describes the access policies of a selection of pharmaceutical companies that have important cancer drug portfolios or cancer drug development projects. The information for this section was collected through research on companies' websites and other publicly available sources. Pharmaceutical companies have a responsibility to make their products available to those in need. Growing demand for cancer care in low- and middle-income countries requires companies with cancer drug portfolios to develop access strategies.

Roche¹⁰²

Roche is by far the most important player in oncology with an annual turnover in anti-cancer drugs of more than \$20bn. Roche's strategy with regards to access to medicines in the developing world is set out in the document 'Access to Healthcare –Roche's global commitment'. According to this document, the aim of the company *'is for every person who needs our products to be able to access and benefit from them'*. The paper goes on to say that *'Roche shares a joint responsibility with governments, international organizations and the rest of our industry to tackle the challenges of improving access to quality healthcare.'* The four key elements of Roche's approach are: 1) delivering innovation; 2) improving affordability; 3) strengthening healthcare infrastructure; and 4) increasing awareness and patient support. Roche lists the following approaches for improving affordability:

- securing reimbursement through commercial arrangements and/or differential pricing;
- assisting patients who pay out-of-pocket through patient assistance programmes;
- contributing to the development of private health insurance coverage.

With regards to intellectual property, Roche does not apply for new patents on any medicine in LDCs and low-income countries. For HIV medicines Roche does not enforce patents in Sub-Saharan Africa (Roche has only one ARV in its portfolio which is not part of the WHO recommended regime), and it practises 'no-profit' pricing. There is no mention of similar approaches to cancer drugs.

Roche is in the process of establishing differential pricing programmes for their therapies, including anti-cancer drugs, in low- and middle-income countries. In the Philippines, Roche is experimenting with a tiered pricing scheme for Herceptin that is linked to the individual patient's ability to pay, as assessed by a third party. There is no information publicly available about the price levels that have been set, nor the outcome of the programme. However, based on information from a blogger/journalist in the Philippines writing about

his mother's treatment it seems that the cost for a two-year treatment course with Herceptin is about \$17,000.¹⁰³ Roche points out that there are many challenges with implementing differential pricing, identifying the use of international reference pricing as a concern. Roche calls for global solidarity to ensure that lower prices granted to low- and middle-income countries are not taken advantage of by high-income countries. They want to see inter-governmental action to ensure that reference pricing and parallel trade are not used outside groups of countries of the same economic development level.

Another approach to differential pricing is through 'second brands' which means that the same product has a different brand name and packaging from the original Roche product. Examples of a cancer drug second brand includes Herclon, a renamed and repackaged brand of trastuzumab (Herceptin) provided by Emcure in India, following an agreement with Roche.

Novartis

Novartis describes its access policy as follows: '*...enhancing access begins with medical research, continues with product donations and new business models, and is supported by action to strengthen healthcare in both developing and advanced economies.*'¹⁰⁴

It lists the following as key components of its support to patients in need.

- Patient assistance programmes, such as the Glivec Global Patient Assistance Program and the Gleevec US Patient Assistance Program, which provide Glivec/Gleevec free or at reduced cost to patients in need.
- Considering differential pricing possibilities for essential drugs on a case-by-case basis, such as the malaria treatment Coartem for public-sector use in developing countries, at an average cost of less than \$1 per treatment.
- Donations for diseases such as leprosy, tuberculosis (TB), and liver fluke.
- Research against 'neglected' diseases that predominantly afflict patients in developing countries.
- The Novartis Foundation for Sustainable Development develops and implements innovative strategies and programmes to deliver health services to impoverished people.
- New business models such as our Arogya Parivar¹⁰⁵ programme – a for-profit healthcare social initiative active in rural India.

With regards to cancer medication access, and in the context of this report, Novartis's direct-to-patient access programme – the Glivec International Patient Assistance Program (GIPAP) for patients with CML (chronic myeloid leukaemia) or GIST (gastrointestinal stromal tumour) – is most relevant. The programme was launched in 2001. According to Novartis, GIPAP is active in over 80 low- to middle-income countries, and donates to patients who are not insured, not reimbursed, cannot pay for the treatment privately and are in countries that have minimal reimbursement capabilities. It has provided free imatinib (Glivec) to 16,000 patients in India.

GIPAP is carried out by The Max Foundation, a small NGO based in the US with partners in 43 countries administering the programme. The Foundation is the company's key collaborator in the administration of GIPAP globally. In 2003 the New York Times criticized Novartis for using the programme to prevent generic supply by threatening to stop its donations when generic versions of the medicines are made available, and to enlist patients to lobby for reimbursement of the drug.¹⁰⁶

Novartis's preferred approach to access issues is the use of donations. In the case of cancer medicines they use direct-to-patient donations, which involve case-by-case management. Drug donations can never provide a sustainable answer to the current cancer care crisis in low- and middle-income countries.

Differential pricing is only practised in the case of the antimalarial drug Coartem – which is a second brand of the antimalarial drug artemeter/lumefantrine sold under the brand Riamet for travellers from high-income countries.

The company does not have an access policy with regards to its patents. Novartis specifically states that patents are not a main barrier to access and mentions the lack of access to non-patented essential medicines on the WHO Essential Medicines List as evidence for this statement. Novartis is open to licensing of their patents for neglected tropical diseases research only.¹⁰⁷ Its website does not list any other patent licensing for access opportunities.

Sanofi-Aventis¹⁰⁸

Sanofi has a dedicated Access to Medicines (ATM) department which focuses on malaria, tuberculosis, neglected tropical diseases (sleeping sickness, leishmaniasis, Chagas disease, Buruli ulcer), epilepsy, and mental disorders. For these diseases Sanofi has medicines in its portfolio. The programme does not mention cancer. Sanofi's central approach to affordability is through 'a differentiated pricing policy to help ensure medicines are affordable for all'. And to 'Adapt our commercial offering based on the economic conditions in the countries we seek to help'.

Cancer is mentioned in the context of support programmes for prevention, diagnosis and follow-up, for chronic diseases (e.g., cancer, diabetes and mental illness). But the website does not list a programme or outlines an approach to provide access to Sanofi's cancer medicines.

Genzyme, a Sanofi biotech company, works with Project Hope and the National Cancer Coalition to donate medicines. It provides the following information about access to its products in developing countries:

Outside the United States, medical care is often managed and funded by national governments. In such countries, Genzyme works closely with governments to help facilitate approval of our treatments and ensure that they are accessible to citizens covered by national health services (Genzyme.com).

In developing countries, we help physicians and local authorities build sustainable health care systems that can pay for critical treatment.

Where such systems do not yet exist, we provide free treatment to patients in the interim until longer-term, sustainable solutions can be established locally.

If you live outside the U.S. and need assistance getting or paying for treatment, talk to your health care providers or a local patient organization. You can also contact Genzyme in your region.

One of the company's recent partners is the National Cancer Coalition (NCC), a non-profit that has expanded beyond its original focus on cancer to help us reach patients in Latin America. The NCC's strong regional presence and local relationships help the company import medicine into some countries in the region, deliver it to patients, and monitor their ongoing progress and needs.

Bristol-Myers Squibb

Bristol-Myers Squibb, according to its own website, is a global BioPharma company that is producing medicine to help patients in their fight against major diseases, including cancer.

The company says it is committed to providing patient access to healthcare. It works towards that goal through public/private partnerships like Secure The Future, and through its Patient Assistance Programmes which provide free medication to 'qualifying patients with financial hardship' in the US.

On access to medicine in the developing world, the company claims to work closely with government health authorities and other payers in seeking marketing authorization and reimbursement for therapies, while also relying on a number of companywide policies, programmes, and innovative initiatives to guide their efforts.

Bristol-Myers Squibb stresses 'with particular importance, the pressing need for medications produced by this company in low-and middle-income countries in the developing world.' However, details of how the company tries to meet this need are not provided. Secure the Future is a Bristol-Myers Squibb Foundation that focuses on HIV/AIDS only and does not deal with cancer. Since 1999 the foundation has allocated \$150m in grants for medical research and care and community support. It is not an access to medicines programme as such.

BMS groups its 'access to medicines in the developing world' efforts under 9 different areas (<http://www.bms.com/responsibility/access-to-medicines/Pages/default.aspx>). The three areas 'pricing and assistance', 'access management', and 'patent, licensing and technology transfer' are most relevant to this report.

The area 'pricing and assistance' lists the following with regards to access to cancer medication.

India. Through a third-party patient support agency 'Oasis', improve compliance and medicine availability for patients with CML.

Argentina, Peru, Chile, Colombia. Provide compassionate use of oncology products through physicians.

Russia. The site mentions 'numerous activities' to improve patients' therapy adherence.

Through the 'Bridging Cancer Care' programme of the Bristol-Myers Squibb Foundation, seven initiatives to improve cancer care in Russia are supported by Foundation grants. The grants, totalling \$1m, focus on improving the capabilities of nurses in cancer care.

The area 'patents, licensing and technology' lists a number of initiatives which are almost all related to HIV or HIV/TB co-infection, as well as one in neglected tropical diseases. There is no mention of licensing of patents or other measures to help increase access to BMS's anti-cancer drugs.¹⁰⁹

The activities listed in the area 'access management' describe the HIV global access programme and direct patient access to investigational drugs. It is not clear whether this programme, implemented by the UK-based Direct Import Programme: Idis, includes oncology products.

The website does not provide information about the number of patients that have been able to benefit from access to cancer treatment under the listed activities.

Bayer

Bayer has patient assistance programmes for kidney cancer and liver cancer patients in countries of South and Southeast Asia, in Brazil, and several countries in South Eastern Europe. In 2008, Bayer implemented a Patient Assistance Programme in India along with the market launch of sorafenib (Nexavar) in the Indian market. According to the Bayer website, the programme reduces the cost of the monthly treatment of the patented Bayer drug therapy for qualified patients enrolled, to about 10 percent of the regular pharmacy price for the complete duration of treatment.¹¹⁰

According to MSF, Bayer's access programme requires the patient to pay Rs. 30,000 (\$493) for the first three days of the month then the patient can access sorafenib from Bayer free for the next 27 days. Bayer's access programme's cost of Rs. 30,000 per patient per month is still 4.5 times higher than the cost of the generic sorafenib (Rs. 6,840 -\$110).¹¹¹

Conclusion

Drug companies' policies for access to cancer drugs do not seem to be well developed. The contrast with the publicized access programmes for HIV is notable. Companies' access approaches for cancer lean heavily on traditional drug donations/charitable approaches and are often on a case-by-case basis. For example, none of the websites mention licensing approaches for cancer

drugs. Roche's experimentation with second brand production of trastuzumab by Emcure in India comes closest to a licensing approach.

Differential pricing can be interesting if the different pricing levels indeed reflect the ability of the target population to pay. In reality this is hardly ever the case as is illustrated by the case of Herceptin in the Philippines. GSK announced last year two-tiered priced cancer drugs for the Indian market: eltrombopag (Revolade) to increase platelet production in patients with serious blood disorders, priced at Rs. 27,000 (\$444) and pazopanib (Votrient) used in the treatment of advanced kidney cancer at Rs. 58,000 (\$954) a month. India's GNI per capita is \$3,820 or \$318 per month which shows that these tiered prices do not reflect the ability to pay nor the fact that most people in India pay for healthcare out-of-pocket.

Concerns about differential pricing being used in international reference pricing may sound legitimate – but the evidence from HIV pricing does not, in fact, support those concerns. Companies have maintained their high prices for ARVs despite differential pricing programmes. As long as cancer drug prices are seen as unsustainable in high-income countries, it may be difficult to gain support for a global agreement that limits the use of reference pricing. Nevertheless, Roche's proposal to reach a global agreement on reference pricing based on groupings of countries with similar levels of economic development should be further explored if this could indeed lead to affordable medicines and not ring-fencing of markets to maximize profits in each.¹¹²

The companies' websites give the impression that none of them has a coherent approach to access to cancer medication for people in low- and middle-income countries. The statement by the CEO of Bayer – that they had not developed the cancer drug Nexavar (sorafenib) for the Indian market, but '*for Western patients who can afford the product*', is refreshingly honest and confirms that the focus of the industry is on wealthy markets and not on people in need. For this to change the business model of the industry will need to change drastically.

The information in this chapter is based on publicly stated policies provided by the companies on their websites. More in-depth exploration may be needed to gain a full picture of companies' approaches to increasing access to cancer medications.

6 COUNTRY STRATEGIES AIMED AT DECREASING THE PRICES OF CANCER DRUGS

I think compulsory licenses will be on the rise all over the world because it is the middle path between extreme patent protectionism and patent abolitionism. Shamnad Basheer¹¹³

Since the adoption of the Doha Declaration on TRIPS and Public Health in 2001, countries have used the TRIPS flexibilities to access lower-priced generic medicines. For example, compulsory licensing, including government

use licenses and non-enforcement of patents by LDCs has been widespread in the procurement of AIDS medicines. India and Thailand are the only countries that have used compulsory licensing for cancer medication.

India

Compulsory licensing of cancer drugs

India is home to generic drug producers that are capable of making low-cost cancer drugs. When a product is patent protected a generic company can only make a copy if it has a license to do so. This can be a voluntary or non-voluntary (compulsory) license. Non-voluntary or compulsory licenses allow generic versions of cancer medications to be produced despite the existence of a patent. In general, generic versions of medicines are less costly than the originator's product. The Ministry of Health recommended, in January 2013, compulsory licensing of the patents on three anti-cancer drugs, dasatinib, trastuzumab, and ixabepilone¹¹⁴ to the Department of Industrial Policy and Promotion (DIPP).¹¹⁵ To date India has granted a CL for the cancer drug sorafenib tosylate to treat liver cancer following a request from generic manufacturer Natco under Section 84 of the Indian Patents Act.¹¹⁶ This CL marked India's first CL for a medicine and is so far the only one.

Table 10 – Patent disputes in India involving cancer drugs

Product	Patent holder	Patent application date India	Date CL application	Grant/Rejection CL	Licensee/Applicant/opponent	Royalty	Legal status
Sorafenib tosylate (Nexavar)	Bayer		2011 (Sept.) ¹¹⁷	2012 (March) ¹¹⁸ 2013 (March) CL upheld	NATCO (CL)	6% raised to 7% (2013 by IPAB)	Bayer's appeal rejected by IPAB (4/3/13). Bayer announced plans to appeal the decision.
Dasatinib (Sprycel)	BMS		2013 (March)	CL request Rejected 30 Oct. 2013 ¹¹⁹	BDR (CL)	NA	CL request rejected by Indian patent controller
Trastuzumab (Herceptin)	Roche		2013 (Jan.)		NA	NA	Patent lapsed
Ixabepilone (Ixempra)	BMS		2013 (Jan.)				Recommended for CL by expert panel of MoH
Sunitinib (Sutent)	Pfizer	2002* (Aug) mailbox 2007 patent grant			Patent oppositions by Cipla, NATCO		Patent revoked non-obviousness grounds. (June 2007)
Imatinib (Gleevec/Glivec)	Novartis	1998* (July)					Patent rejected non compliance section 3(d) (April 2013)

*pre-2005 mailbox applications.

Box 8 – Compulsory licensing of biologics

The development and production of biosimilar biotechnology products by generic companies require considerable investments. Generic companies are not likely to make such an investment if they are not assured that patent barriers are cleared away. Civil society organizations in India have argued that the announcement of the government's intention to issue compulsory licensing will stimulate the investment by companies into the development of biosimilar cancer medications.¹²⁰ Civil society also recognized technological challenges in the production of biosimilars and, for example, with regards to trastuzumab, they asked the government of India to establish a high-level inter-ministerial task force involving biotechnology experts from publicly funded research organizations and civil society organizations to address the technological issues involved in the production of the drug.¹²¹

Cases of patent grant opposition for cancer drugs

Under Indian law anyone can file an opposition against the grant of a patent by the Indian Patent Controller. Since 2006, generic companies and civil society organizations have successfully used these so-called pre- and post-grant oppositions to prevent the grant of patents for certain medications. A patent grant opposition has been successful in the case of cancer drugs; the most prominent was the imatinib (Gleevec) case. Another successful patent grant opposition concerned the anti-cancer drug sunitinib (marketed as Sutent by Pfizer) used for the treatment of renal and gastrointestinal cancers by Cipla.¹²² This opposition led to the revocation of the patent in question on 24 September 2012 by the patent controller in Delhi.¹²³

Responses from industry – fierce response from US

The first and so far only compulsory license concerning a medicine and successful pre-grant opposition of the Gleevec (imatinib) patent provoked fierce responses from the industry and policy makers, in particular in the US. One hundred and seventy members of Congress wrote to President Obama complaining about the CL for sorafenib and expressing concerns about more CLs to follow.¹²⁴ Forty senators wrote to Secretary Kerry to express similar concerns and Business groups established a new coalition – the Alliance for Fair Trade with India – focusing on India's IP policy.¹²⁵

Thailand

Compulsory licensing for cancer drugs

During 2006–2008 Thailand issued compulsory licenses for seven drugs: efavirenz and the lopinavir/ritonavir (LPV/r) combination (which are antiretroviral drugs); clopidogrel (for the treatment of coronary artery disease); and four anti-cancer drugs: letrozole (early breast cancer), docetaxel (breast cancer), erlotinib (small-cell lung cancer), and imatinib (CML). Prior to the granting of the CLs, a series of price negotiations took place with the patent holders. However, the price reductions offered were deemed not sufficient or came with unacceptable terms attached. The implementation of the government use license for imatinib was subsequently suspended on

condition that the original drug was provided free to low-income patients under the government health insurance scheme and the Novartis Glivec International Patient Assistance Program (GIPAP).

The Thai CLs were of the ‘government use’ variety. Thai law (Section 51 of the Thai Patent Act BE 2522,) authorizes the government to use patents in the general public’s interest, so that ‘any ministry, bureau or department of the Government’ may exercise the rights in any patent ‘to carry out any service for public consumption’. Government use licenses are fully compliant with international law such as the TRIPS Agreement and are used by many governments, including the US, for various public policy reasons.

The Thai decision to issue compulsory licenses for these medicines was part of a series of cost containment measures that followed the decision to provide universal health coverage in 2011. The Thai universal health coverage plan extends healthcare to many poor Thai citizens and entitles those covered under the plan access to the medicines contained in the National List of Essential Medicines (NLEM). In 2003, Thailand also decided to provide universal access to HIV treatment.

Table 11 – Prevalence of patients with cancer in Thailand

Type of Cancer	N patients (2004)
Breast cancer	28,426
Lung cancer	12,549
Stomach cancer	3,589
Leukaemia	1,107

Source: Burden of Disease and Injury Project Database, IHPP, Thailand.

Table 12 – Incidence of cancer in 2004 and 2012 in Thailand (projected)

Type of Cancer	2004	2012
Breast cancer	9,763	16,765
Lung cancer	9,001	12,176
Stomach cancer	2,030	2,624
Leukaemia*	2,152	3,078

*Within the number of patients in the Leukaemia registry, approximately 10–18 percent have chronic myeloid leukaemia (CML) mostly aged under 20 years old.

The Thai Health Intervention and Technology Assessment Program (HITAP) carried out an assessment of the effects of the compulsory license measures focusing on health impact, health-related economic impact, impact on trade and foreign investment. The study also included a survey of the views of key Thai and international stakeholders to assess the psychosocial impact: healthcare workers, researchers/academics and civil servants, government officials, the private sector, non-governmental organizations (NGOs) and foreign stakeholders.¹²⁶ It is interesting to note in the context of this study that the stakeholders interviewed about the Thai CLs were more supportive of the use of such a measure for HIV than for NCDs. One explanation for this is the common misunderstanding that CLs are not legal unless there is a state of emergency or extreme urgency and, therefore, not suitable for use in chronic

non-communicable diseases.

The assessments carried out by HiTAP show clear benefits in terms of access to treatment. The study estimated the increase in the number of patients with access to the four anti-cancer drugs over the five-year study timeframe as follows: 8,916 patients for letrozole; 10,813 for docetaxel, 1,846 for imatinib; and 256 for erlotinib.

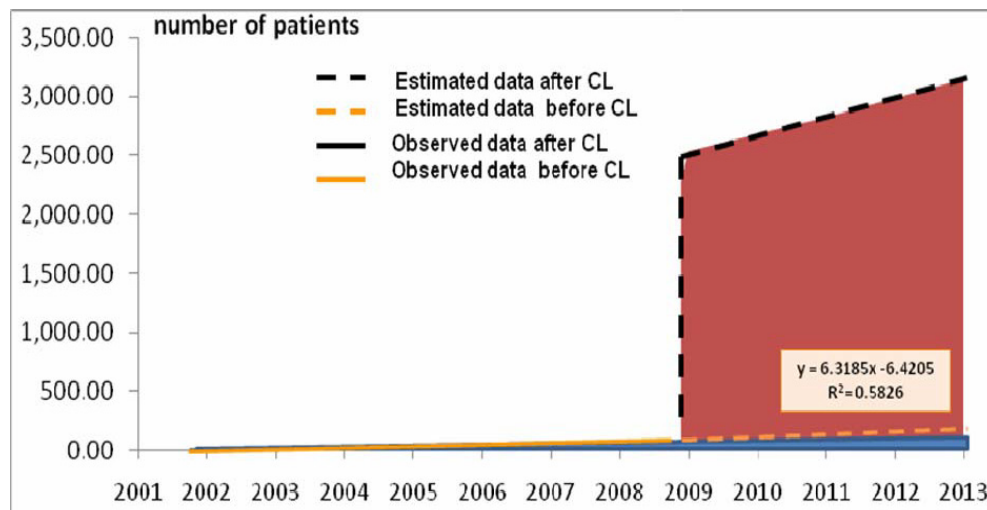
The results, in terms of QALYs gained as a result of the CLs were as follows (in order of drugs with the greatest health gains):

- Letrozole: 3,656 QALYs gained;
- Imatinib: a total of 2,435 QALYs gained (1,384 QALYs for Chronic Myeloid Leukemia (CML) patients; 1,051 QALYs for Gastrointestinal Stromal Tumor (GIST) patients);
- Docetaxel: 1,251 QALYs gained.

There was no QALY data was available for erlotinib.

Considering that these medicines are used to fight life-threatening diseases, not issuing these government use licenses and extending the availability of the products to people suffering from cancer would have been inhumane. The following chart shows the number of patients with breast and lung cancer who gained access to treatment as a result of the government's action.

Graph 3 – Increase in number of patients with access to docetaxel to treat breast and lung cancers following grant of government use license (GUL)



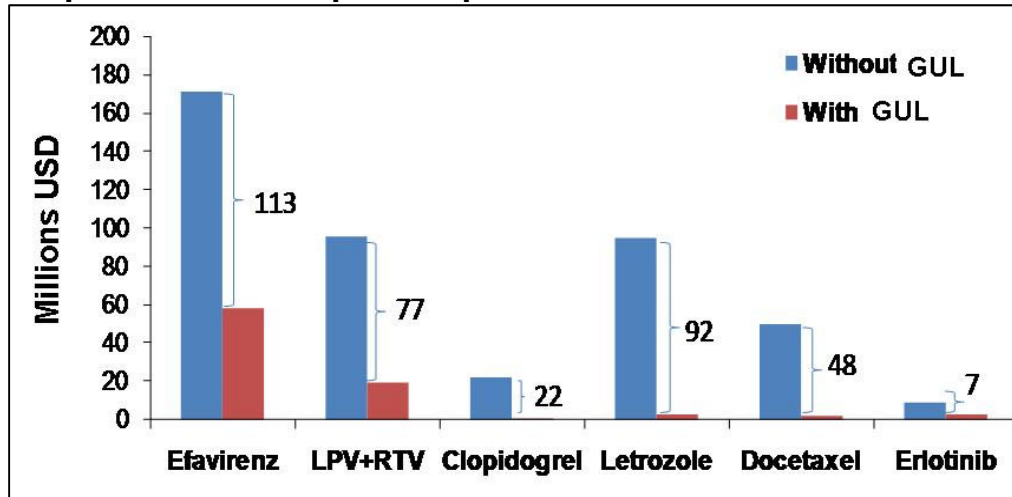
Source: Thai Ministry of Health, May 2009.¹²²

Effects on export trade and foreign direct investment

Domestic criticism was often driven by a concern for adverse economic effects as a result of trade sanctions by trading partners such as the US. Thailand's trade status was downgraded by the US from the 'Watch List' (WL) to the 'Priority Watch List' (PWL) under the Special 301 provisions for intellectual property violations. The US also withdrew three Thai export products from the Generalized System of Preferences (GSP) in 2007 but granted GSP status to eight new products in the same year. The GSP

withdrawal did, therefore, not adversely affect the overall export status. The study also did not find any adverse effects on foreign direct investment. In summary, the study found no short-term adverse economic effects of CLs.

Graph 4 – Price comparison products without and with CL 2007–2012



Source: Thai Ministry of Health quoted in: http://unctad.org/Sections/dite_totip/docs/tot_ip_0018_en.pdf

In conclusion, CLs for HIV and cancer drugs in Thailand have been important for increasing access and lowering the cost of patented medicines, with no short-term adverse economic effects.

7 CONCLUSIONS AND RECOMMENDATIONS

The fact is that two-thirds of the world's extreme poor are concentrated in just five countries – India, China, Nigeria, Bangladesh, and the Democratic Republic of Congo. If you add another five countries – Indonesia, Pakistan, Tanzania, Ethiopia, and Kenya – the total grows to 80 percent of the extreme poor.

Jim Yong Kim, World Bank Group President, 1 April 2014¹²⁷

Cancer is on the rise globally because of changing demographics and changing lifestyles. Currently 14 million people a year are diagnosed with cancer. That will increase to 19 million by 2025, 22 million by 2030, and 24 million by 2025. More than 60 percent of the world's cancer cases occur in Africa, Asia, and Central and South America. Breast cancer is on the rise globally and has become a leading cause of cancer death in low- and middle-income countries. Planning for screening and treatment of cancer in low- and middle-income countries is lagging behind. Any strategic approach towards increasing access to cancer treatment needs to take into account the cost as well as the complexity of treatment, and include measures to ensure access to low-cost cancer drugs of assured quality.

The problem of high pricing of cancer medications is a global challenge. While problems with access to cancer treatments are most serious in low- and middle-income countries, they are by no means confined to those countries. See section 2.1. Equitable pricing, and access strategies for low- and middle-

income countries, will benefit from more sustainable pricing in high-income countries. For example, the industry's concern about flow back of lower priced medicines to high-income markets or the use of reference pricing by high-income governments may be legitimate. But it will be easier to gain political support for solutions if the prices charged for new cancer medicines were more affordable in high-income countries.

The industry will maintain that research and development of new medicines is dependent on high prices, and that any restrictions will hurt new drug development. This is the current model for innovation: companies invest part of their earnings into R&D for new products. Since this innovation model leads to access problems, it seems necessary to look at alternatives to high prices as the main means to fund R&D. One such alternative model is changing the relationship between the cost of R&D and the price of the product, which has become known as 'delinkage'. One way to accomplish this goal is through prize funds. In 2011 US Senator Sanders proposed an \$80bn prize fund for pharmaceutical innovation that would replace monopolies with prizes.^{128,129} In 2008, Bolivia and Barbados developed a proposal for a prize fund for cancer drugs for developing countries. They proposed that developing country governments introduce a system for rewarding the development of new medicines and vaccines against cancer that would permit free entry by generic suppliers for vaccines and medicines, avoiding monopoly control. In return for ending the monopoly, the governments should agree to provide a domestic system of rewards for developers of new products that is funded through a fixed proportion of the budget for cancer (other bases for financing were suggested).¹³⁰ However, since 2008 nothing has happened with these recommendations.

More recently, the European Federation of Pharmaceutical Industries and Associations (EFPIA) has acknowledged that delinking payment for R&D costs and prices can be a viable model in certain cases, for example to incentivize the development of new antibiotics. EFPIA is willing to experiment with delinkage in special cases, but does not embrace a more general application.

After the report of The WHO Consultative Expert Working Group appeared, WHO solicited proposals for R&D demonstration projects. WHO required that projects address new financing methods and specifically asked for projects that promote delinkage of the cost of research and development from the product price (see Box 9).

Box 9 – R&D demonstration projects

Demonstration Projects are aimed at developing health technologies (medicines, diagnostics, medical devices, vaccines, etc.) for diseases that disproportionately affect developing countries and for which identified R&D gaps remain unaddressed due to market failures. The projects must demonstrate effectiveness of alternative, innovative and sustainable financing and coordination approaches to address identified R&D gaps. The selection of projects will be based primarily upon the following considerations:

- they address research and development gaps related to discovery, development and/or delivery of health technologies for diseases that disproportionately affect developing countries, particularly those living in poverty, and for which immediate action can be taken;
- they utilize collaborative approaches, including open-knowledge approaches, for research and development coordination;
- they promote the delinkage of the cost of research and development from product price; and
- they propose and foster innovative financing mechanisms.

Source: http://www.who.int/entity/phi/demonstration_projects/en/index.html

Several R&D demonstration projects were submitted to WHO for the development of cancer drugs. The 22 projects shortlisted by WHO's regional committees do not include cancer projects and the projects that will be considered by the WHO's Executive Board in 2014, with one exception, only concern tropical neglected diseases offering little new in terms of models for financing of medical R&D that could help break the cycle of high drug prices.

To break the cycle of ever-higher drug prices needed to sustain the costs of R&D, new models for the financing of R&D need to be explored. Such models should have, as a guiding principle, that they equitably serve both health driven R&D and access to the innovations that are a result of such R&D. The current debates at WHO in the context of the WHO Global Strategy and Plan of Action on Innovation, Public Health and Intellectual Property offer a platform for exploring new models. But opposition from powerful industries and their home governments, strongly attached to monopoly ownership, is likely to be fierce. To counter such opposition it will be important that low- and middle-income countries make proposals based on burden sharing of the cost of R&D. If all contribute, all should benefit.

Cancer is on the rise in low- and middle-income countries. However, in these countries, treatment for cancer is often not widely available. Only 5 percent of the global resources for cancer are spent in the developing world, yet these countries account for almost 80 percent of disability adjusted years of life lost to cancer globally.¹³¹ Increasing access to effective cancer treatments in low- and middle-income countries requires the development and implementation of comprehensive cancer prevention, detection, treatment and care policies that include palliative care and pain control. Non-price barriers to access to opioids, for example, continue to be a problem in many developing countries thrown up by international agreements targeting illicit trade in narcotic drugs.¹³²

There is an urgent need for advocacy for cancer care at the national and international level. We have seen the strong role of civil society, the media and health professionals as advocates for HIV treatment. In particular the development of strong civil society in countries like India, Thailand, South-Africa, and other middle-income countries will be necessary.

Today, global action to increase efforts towards prevention and treatment of NCDs falls far behind the need.¹³³ There are, however, important international

policy developments that can help stimulate action towards prevention, treatment and care in the field of cancer and help bring the cost of treatment down. Some examples are:

- The **Global Task Force on Expanding Access to Cancer Care and Control**, established in 2009, published in its report in 2011 a wealth of data and recommendations for action. These recommendations include bringing cost down of cancer medicines, emphasizing how to deal with high-priced patented cancer drugs. The Task Force has mobilized many actors in the cancer field.^{134,135}
- The **UN Summit on prevention and control of non-communicable diseases**¹³⁶ has put the spotlight on the need to close the divide in cancer care. Hogerzeil et al. have drawn attention to the lessons from HIV in lowering the price of treatments that may be applied for high-cost patented medicines for NCDs, such as cancer.¹³⁷ The summit has elevated the attention to NCDs in low- and middle-income countries and highlighted the need to provide access to treatment.
- The drive towards **Universal Health Coverage (UHC)** is picking up speed. The goal of universal health coverage is to ensure that all people obtain the health services they need without suffering financial hardship when paying for them. According to WHO this requires:
 - a strong, efficient, well-run health system;
 - a system for financing health services;
 - access to essential medicines and technologies;
 - a sufficient number of well-trained, motivated health workers.

It is generally recognized that UHC will require that efforts to control the cost of treatments are successful.

These global developments are important to create the political momentum to strengthen healthcare for cancer patients at national level and take action globally to provide guidance for treatment and care, share knowledge about treatment cost and provide a legal framework to ensure treatment is available.

Box 10 – Specific recommendations for India

India should develop a national cancer policy for the prevention, diagnosis, and treatment of cancer. Such a policy should pay special attention to payment for care since most people in India today pay out-of-pocket. According to the Indian Commission on Macroeconomic and Health Financing, at least 70 percent of payments for healthcare come from household budgets. A comprehensive cancer prevention and care policy should include addressing pricing of cancer medicines. The focus on price of medicines alone is of limited value without a true commitment to such a policy.

India is home to important pharmaceutical companies that are capable of producing low-cost quality cancer medicines. A rational selection of products

for use in the national healthcare system will help create markets for essential cancer products, many of which are not patented in India. India has signalled its willingness to provide compulsory licenses for patented cancer medication. The selection of candidates for compulsory licensing should be driven by health needs and a national policy. The development of an essential cancer medicines list for India would help to guide India's IP policies, allowing its generic companies to plan ahead. Compulsory licenses for the production of generic cancer medication should allow production for export to countries that lack access to these medicines and do not produce them themselves.

Specific recommendation to improve access to cancer medicines

Ensuring the availability of affordable cancer treatment will be a key element in efforts to expand treatment access to many people who need it. The following recommendations for action specifically deal with access barriers to cancer medication.

➤ **WHO to Develop Standard Treatment Guidelines (STGs) for cancer**

It is important that WHO develops and disseminates standard cancer treatment guidelines for use in low and middle-income countries. STGs provide important guidance to national health authorities and help them make rational decisions about treatments and procurement of health products.

There is today much opportunity to expand access to cancer care with existing low-cost products. Breast cancer provides an important example. Twenty percent of breast cancer patients require trastuzumab (Herceptin) that is prohibitively expensive today. Eighty percent of breast cancer cases can be treated with older, less costly medicines. It is essential that governments take action to ensure the price of trastuzumab comes down. But equally important is making cancer care with less costly medicines available. Advocating for affordable trastuzumab will be more effective in an environment where breast cancer treatment and care is available to all women.

➤ **WHO to make inclusion of cancer medication in the WHO Model List of Essential Medicines a matter of urgency.**

Inclusion of a medicine in the WHO EML is important for a number of reasons:

- it guides countries in rational selection of the most appropriate medicines and thus helps rational and efficient procurement;
- it helps create a market for such medicines;
- it guides the prequalification of the quality of medicines.

In 2013 the WHO Expert Committee recommended a review of the oncology section of Essential Medicines List. This review should take place urgently. It will be an opportunity to include proven effective treatments (regardless of cost) and provide a basis for further action to ensure availability and affordability of these essential cancer medicines. Once cancer medications are included in the core list, such a list can form the basis for inclusion in the World Health Organization's Prequalification Program's Expression of Interest, help attract low-cost quality generic suppliers and guide countries' selection.

➤ **Establish WHO Prequalification for cancer medication**

Prequalification of HIV medicines has helped to create the market of quality antiretroviral treatments. The same should happen for anti-cancer drugs. WHO should be asked to expand its prequalification programme and include essential cancer medications on its expression of interest list. WHO should also provide technical guidance for the regulation of biologics.

➤ **Create transparency of cancer drug prices and availability**

HIV has shown us that transparency of prices and sources of essential medication is essential in bringing cost down and ensuring rational, efficient procurement. An overview of price ranges by the Global Task (see Table 3) shows wide ranges in prices paid for cancer medications in low- and middle-income countries. Publicly available drug price and source information should be made available and regularly updated.

➤ **Stimulate low-cost generic production**

Given their strong manufacturing capacity and ability to commercialize affordable health products, countries like Brazil, China, India, and Mexico have the opportunity to serve the world as they prepare to manufacture generic products for cancer. In the cases where generic manufacturing is not possible because of a patent, licenses should be made available. Patent holders should be incentivized to license their patents of essential cancer drugs to generic manufacturers. The Medicines Patent Pool can provide a model for health-oriented licensing and licensing terms. Licenses with a large geographical scope help to create economies of scale and thus lower the cost of production. Governments should provide compulsory licenses to generic producers in the case a patent holder refuses to license on reasonable terms. It will be important to protect the flexibilities in intellectual property law that countries have to remedy the negative effect of drug patents. The use of these flexibilities to increase access to cancer drugs is completely legal under international law. Current TRIPS Plus demands by the US and EU in trade agreements risk, nevertheless, eroding existing policy and legal options. Countries have to intervene when patents cause access problems and patent holders refuse to provide licenses to the patents.

➤ **Ensure sustainable differential pricing**

In cases of a single-supplier product, for example because of a patent, governments should provide incentives to encourage companies to provide cancer medications at significantly reduced prices so they are affordable for low- and middle-income countries. This may require agreements at international level on reference pricing to prevent high-income countries demanding discount levels intended for low- and middle-income countries. A very effective mechanism for differential pricing of patented medicines is through licensing. Production of lower-priced products by generic companies offers the steepest discounts. Because products produced under a license are marketed under a different brand, there is no risk of flow back to high-income markets, which has always been a concern of originator companies in implementing differential pricing.

Demands for cancer treatment in low- and middle-income countries will increase and a response by health authorities in many countries is long overdue. This lack of response cannot be explained by the high cost of cancer medicines only. Many of the products used in cancer treatment are available from multiple sources at affordable price levels. To make those medicines available to cancer patients, governments should put in place, and sustain, cancer screening and treatment strategies.

Newer medicines are often patented and thus only available from one source. This means that there are no generic low-cost equivalents on the market. Those medicines are often very highly priced and out of reach of people and health systems in low- and middle-income countries. Essential cancer medicines whether old or new, should be made available in the context of cancer care. This will require action by governments and companies to ensure these treatments are affordable.

From HIV we have learnt which mechanisms for bringing the price of medication down work and which ones do not. For some cancer medicines robust generic supply exists. In case of single-source cancer drug supply, relying on differential pricing alone does not provide the sustained decrease in price that is necessary. Robust generic supply of quality is essential. This will require action from WHO to include cancer medication in the Essential Medicines List and to offer prequalification of such medicines. Where patents are barriers to access generic cancer medication, companies should offer licenses and if they fail to do so governments should use compulsory licensing strategies. However, for all of this to happen we need a vocal civil society that demands drastic change in the current situation.

Tables, Graphs and Boxes

- Table 1 – Sales of the 10 leading companies in the global cancer market 2010* and most important products of the top five companies
- Table 2 – FDA-approved drugs discovered through public-sector research, according to type of review and chemical type, 1990–2007
- Table 3 – Indicative chemotherapy and hormone therapy costs for selected essential medicines for cancer in low- and middle-income countries
- Table 4 – Average price of six cancer drugs in four countries
- Table 5 – Price of trastuzumab in \$ for 1 year course
- Table 6 – Retail price of Letrozole in India (per tablet 2.5mg)
- Table 7 – Clinical trials sponsorship
- Table 8 – Retail price Dasatinib 50mg tablet
- Table 9 – Pharmaceutical market growth by region
- Table 10 – Patent disputes in India involving cancer drugs
- Table 11 – Prevalence of patients with cancer in Thailand
- Table 12 – Incidence of cancer 2004 and 2012 in Thailand (projected)

- Graph 1 – Cost of imatinib brand Gleevec (blue bars) and cost of generic imatinib per patient per month
- Graph 2 – The evolution in price of different first line regimens
- Graph 3 – Increase in number of patients with access to docetaxel to treat breast and lung cancers following grant of government use license (GUL)
- Graph 4 – Price comparison products without and with CL 2007–2012

- Box 1 – Call for action on cancer drug prices
- Box 2 – Breast cancer
- Box 3 – Section 3(d) Indian Patents Act
- Box 4 – Leukemia
- Box 5 – The case of Taxol
- Box 6 – Biosimilars and trade agreements
- Box 7 – Expanding access to affordable cancer care
- Box 8 – Compulsory licensing of biologics
- Box 9 – R&D demonstration projects
- Box 10 – Specific recommendations for India

Notes

All URLs in this section were last accessed in May 2014.

- ¹ New Global Cancer Country Profiles, <http://www.who.int/cancer/en/index.html>
- ² C. de Martel, J. Ferlay, S. Franceschi *et al.* (2012) 'Global burden of cancers attributable to infections in 2008: a review and synthetic analysis', *The Lancet Oncology* 13: 607–615.
- ³ Anne Gulland (2014) 'Global cancer prevalence is growing at "alarming pace," says WHO' <http://www.bmj.com/content/348/bmj.g1338>
- ⁴ M. Roberts 'Cancer: A global threat', <http://www.bbc.com/news/health-26031748>
- ⁵ A disability adjusted life year can be thought of as one lost year of healthy life. See: http://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/
- ⁶ Global Task Force on Expanded Access to Cancer Care and Control, <http://gtfcc.harvard.edu/icb/icb.do?keyword=k69586&tabgroupid=icb.tabgroup138264>
- ⁷ CEO of GSK at the annual general meeting of the Organization of Pharmaceutical Producers of India (OPPI) in 2011 <http://www.scripintelligence.com/home/The-Glivec-calculus-what-changed-after-the-hype-341824>
- ⁸ India's per capita GDP, for example, is \$1500.
- ⁹ T. Fojo, C. Grady (2009) 'How much is life worth: cetuximab, non-small cell lung cancer, and the \$440 billion question', *J Natl Cancer Inst.* 101(15): 1044–1048.
- ¹⁰ E. 't Hoen (2013) '[A victory for global public health in the Indian Supreme Court](#)', *J Public Health Policy* 34(3): 370–4. doi: 10.1057/jphp.2013.21. Epub 2013 May 16. PubMed PMID: 23677206.
- ¹¹ *The Economist* (2011) 'Drug companies in America. The costly war on cancer. New cancer drugs are technically impressive. But must they cost so much?' *The Economist*, 26 May. <http://www.economist.com/node/18743951>
- ¹² Ebola virus: American govt scales up Ebola response in West Africa, <http://www.afriquejet.com/news/11958-cancer-treatment-nigerians-pay-for-cancer-treatment-with-their-lives.html>
- ¹³ Experts in Chronic Myeloid Leukemia (2013) 'The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts', *Blood* 121(22): 4439–42
- ¹⁴ 'Insuring the Future: Current Trends in Health Coverage and the Effects of Implementing the Affordable Care Act' http://www.commonwealthfund.org/~media/Files/Publications/Fund%20Report/2013/Apr/1681_Collins_insuring_future_biennial_survey_2012_FINAL.pdf
- ¹⁵ Study Links Medical Costs and Personal Bankruptcy http://www.businessweek.com/bwdaily/dnflash/content/jun2009/db2009064_666715.htm
- ¹⁶ Peter B. Bach, M.D., M.A.P.P.N (2009) 'Limits on Medicare's Ability to Control Rising Spending on Cancer Drugs' *Engl J Med* 360: 626–633doi: 10.1056/NEJMhpr0807774.
- ¹⁷ P.B. Bach, L.B. Saltz, R.E. Wittes (2012) 'In cancer care, cost matters' *New York Times* 15 October: pA25 (http://www.nytimes.com/2012/10/15/opinion/a-hospital-says-no-to-an-11000-a-month-cancer-drug.html?_r=0).
- ¹⁸ Experts in Chronic Myeloid Leukemia op. cit. doi: 10.1182/blood-2013-03-490003 (<http://bloodjournal.hematologylibrary.org/content/121/22/4439.long>).
- ¹⁹ 'The Price of Drugs for Chronic Myeloid Leukemia (CML); A Reflection of the Unsustainable Prices of Cancer Drugs: From the Perspective of a Large Group of CML Experts' <http://bloodjournal.hematologylibrary.org/content/early/2013/04/23/blood-2013-03-490003.full.pdf>
- ²⁰ 'Generic HIV drugs will widen US treatment net' <http://www.nature.com/news/generic-hiv-drugs-will-widen-us-treatment-net-1.11173>
- ²¹ M. Jackson (2013) 'Gilead critic sponsors voter initiative to limit drug pricing in San Francisco'. <http://www.scripintelligence.com/policyregulation/Gilead-critic-sponsors-voter-initiative-to-limit-drug-pricing-in-San-Francisco-340548>
- ²² 'Prescription Drug Purchasing, Proposition D' http://ballotpedia.org/Prescription_Drug_Purchasing,_Proposition_D_
- ²³ Andrew Jack in London and Kerin Hope in Athens(2013) 'Athens urged to import generic drugs', *Financial Times*, 17 March <http://www.ft.com/intl/cms/s/0/ade78168-8f3a-11e2-a39b-00144feabdc0.html?siteedition=intl#axzz2fuTRmT1R>
- ²⁴ 'Health care in Greece' http://en.wikipedia.org/wiki/Health_care_in_Greece
- ²⁵ Roche Keeps Drugs From Strapped Greek Hospitals <http://online.wsj.com/article/SB10001424053111904491704576574791877220786.html>
- ²⁶ For details on Pompe disease see: <http://ghr.nlm.nih.gov/condition/pompe-disease>
- ²⁷ For details on Fabry disease see: <http://www.ninds.nih.gov/disorders/fabrys/fabrys.htm>

- ²⁸ 'CVZ: dure medicijnen voor drie zeldzame ziektes uit basispakket' <http://www.nrc.nl/nieuws/2012/07/29/cvz-dure-medicijnen-voor-drie-zeldzame-aandoeningen-uit-basispakket/>
- ²⁹ 'Erasmus MC: zelf medicijnen zeldzame ziektes ontwikkelen' <http://www.nrc.nl/nieuws/2012/08/12/topman-erasmus-mc-zet-farma-industrie-buitenspel-reactie-op-advies-cvz/>
- ³⁰ <http://acta.ffii.org/?p=1643> (the original article appeared in the *Volkscrant* of 11 Aug 2012)
- ³¹ 'Exclusive: PCTs 'blacklist' drugs backed by NICE' <http://www.gponline.com/News/article/1105156/Exclusive-PCTs-blacklist-drugs-backed-NICE/>
- ³² 'Michael Rawlins: playing fair on treatments' <http://www.hsj.co.uk/opinion/columnists/michael-rawlins-playing-fair-on-treatments/5047276.article>; 'NHS trusts unlawfully denying patients NICE drugs' <http://www.pharmatimes.com/Article/12-08-07/NHS-trusts-unlawfully-denying-patients-NICE-drugs.aspx>; 'Sue NHS to stop drug rationing: Watchdog urges patients to take action against health trusts which deny them expensive medicine' <http://www.mirror.co.uk/news/uk-news/nice-urges-patients-to-take-action-1214102>
- ³³ A. Hill, S. Khoo, J. Fortunak, B. Simmons, and N. Ford (2014) 'Minimum costs for producing hepatitis C direct-acting antivirals for use in large-scale treatment access programs in developing countries', *Clin Infect Dis.* 58(7): 928–36.
- ³⁴ 'How To Charge \$1.6 Million For a New Drug And Get Away With It' <http://www.forbes.com/sites/matthewherper/2012/03/19/how-to-charge-1-6-million-for-a-new-drug-and-get-away-with-it/>
- ³⁵ 'Natco Pharma wins cancer drug case' <http://www.thehindu.com/business/companies/natco-pharma-wins-cancer-drug-case/article4475762.ece>
- ³⁶ J. Mestre-Ferrandiz, J. Sussex, and A. Towse, (2012) *The R&D Cost of a New Medicine*, London: Office of Health Economics.
- ³⁷ <http://www.pharmalive.com/quote-year-1b-drug-cost-myth>, (last accessed May 2014).
- ³⁸ http://www.pharmamyths.net/files/Biosocieties_2011_Myths_of_High_Drug_Research_Costs.pdf, (last accessed May 2014).
- ³⁹ 'R&D costs for Gleevec' <http://keionline.org/node/1697>
- ⁴⁰ 'Top 10 Best-selling Cancer Drugs' <http://www.fiercepharma.com/special-reports/top-10-best-selling-cancer-drugs/top-10-best-selling-cancer-drugs>
- ⁴¹ Scrip Stats. Scrip Intelligence 2 Oct 2013.
- ⁴² 'Executive Summary for the Economics of TB Drug Development' http://www.tballiance.org/downloads/publications/TBA_Economics_Report_Exec.pdf
- ⁴³ DNDi (2013) 'An innovative approach to R&D for neglected patients. Ten years of experience & lessons learned by DNDi' DNDi: Geneva
- ⁴⁴ 'The Role of Public-Sector Research in the Discovery of Drugs and Vaccines' <http://www.nejm.org/doi/full/10.1056/NEJMsa1008268>
- ⁴⁵ S. Moon, E. 't Hoen (2012) 'Medicines for the World: A global R&D treaty could boost innovation and improve the health of the world's poor—and rich' *Scientist*, <http://www.the-scientist.com/?articles.view/articleNo/32664/title/Medicines-for-the-World/>
- ⁴⁶ Trilateral study by the World Health Organization (WHO), World Intellectual Property Organization (WIPO) and World Trade Organization (WTO) (2013), 'Promoting Access to Medical Technologies and Innovation. Intersections between public health, intellectual property and trade' Geneva: WHO, WIPO, WTO, http://www.wto.org/english/res_e/booksp_e/pamtiwhowipowtoweb13_e.pdf
- ⁴⁷ 'New Global Cancer Country Profiles' <http://www.who.int/cancer/en/index.html>; and 'Cancer Fact Sheets' http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
- ⁴⁸ 'National Cancer Registry Programme' <http://www.ncrpinidia.org>
- ⁴⁹ J. Nangia, and N. Kumar (2005) 'Change in the age structure of India's population (1881-2001)', *Dialogue* 6: 445–457.
- ⁵⁰ R. Takiar, D. Nadayil, and A. Nandkumar (2010) 'Projection of number of cancer cases in India (2010-2020) by cancer group', *Asian Pacific Journal of Cancer Prevention* 11: 1045–1049.
- ⁵¹ K. Nair, C. Varghese, and R. Swaminathan (2005) 'Cancer: current scenarios, intervention strategies and projections for 2015', National Committee on Macroeconomics and Health Background Papers: Burden of disease in India, New Delhi
- ⁵² *Ibid.*
- ⁵³ Planning Commission of India (2011), 'High Level Expert Group Report on Universal health coverage initiative for India', New Delhi: Planning Commission of India.
- ⁵⁴ L. Mithral (1994) 'Breast cancer screening: the case for physical examination without mammography', *Lancet*, 343: 342–344.
- ⁵⁵ K. Nair, C. Varghese, and Swaminathan R. (2005) *op.cit.*
- ⁵⁶ Planning Commission of India *op. cit.*
- ⁵⁷ K. Nair, C. Varghese, and R. Swaminathan *op.cit.*
- ⁵⁸ 'National List of Essential Medicines of India, NLEM 2011' <http://apps.who.int/medicinedocs/en/d/Js18693en/>
- ⁵⁹ 'FDA Approval for Trastuzumab' <http://www.cancer.gov/cancertopics/druginfo/fda-trastuzumab>

- ⁶⁰ Roche (2009) 'Media Release' http://www.roche.com/media/media_releases/med-cor-2009-03-26b.htm
- ⁶¹ 'India partly revokes Roche cancer drug patent' <http://www.reuters.com/article/2013/08/04/us-india-roche-herceptin-idUSBRE97303H20130804>
- ⁶² 'Kolkata Patent office Clarifies ITS Decision on Divisional Applications of Herceptin', Press Information Office Government of India Ministry of Commerce and Industry. 5 August 2013, <http://pib.nic.in/newsite/PrintRelease.aspx?relid=97629>
- ⁶³ 'Roche dropping Herceptin price in India by 30%' <http://www.fiercepharma.com/story/roche-dropping-herceptin-price-india-30/2013-03-01>
- ⁶⁴ 'Biocon to launch world's first Herceptin biosimilar in India' http://www.pharmatimes.com/article/14-01-20/Biocon_to_launch_world_s_first_Herceptin_biosimilar_in_India.aspx#ixzz3QbEB6IAv
Follow us: @PharmaTimes on Twitter
- ⁶⁵ <http://www.bloomberg.com/news/2014-01-20/roche-herceptin-copy-s-price-still-out-of-reach-in-india.html>, (last accessed May 2014).
- ⁶⁶ 'Roche sues Mylan, Biocon and DCGI over Herceptin biosimilar in India' <http://www.biosimilarnews.com/roche-sues-mylan-biocon-and-dcgi-over-herceptin-biosimilar-in-india>
- ⁶⁷ 'Biocon, Mylan get approval for biosimilar of cancer drug Herceptin' <http://www.livemint.com/Companies/ZFFCQ8ZWxl17EeUAmYvuK/India-approves-first-biosimilar-of-Herceptin-made-by-Biocon.html>
- ⁶⁸ Proposal for the Inclusion of Trastuzumab in the WHO Model List of Essential Medicines for the Treatment of HER2-Positive Breast Cancer http://www.who.int/selection_medicines/committees/expert/19/applications/Trastuzumab2_8_2_A_Ad.pdf
- ⁶⁹ The unedited version of the report of the Expert Committee says: Section 8.2 (Cytotoxic and adjuvant medicines) <http://www.who.int/medicines/EC19uneditedReport.pdf>
- ⁷⁰ See also prices presented in KEI's submission to the WHO expert committee on Essential Medicines, see note 67. <https://docs.google.com/spreadsheets/pub?key=0AmviLxGkiHUDdDJTRkx0anBKNo4Z2FkLWVmbFivMGc&gid=2>
- ⁷¹ <http://www.bloomberg.com/news/2014-01-20/roche-herceptin-copy-s-price-still-out-of-reach-in-india.html>, (last accessed May 2014).
- ⁷² National Commission on Macroeconomics and Health, Ministry of Health & Family Welfare, Government of India (2005) 'Report of the National Commission on Macroeconomics and Health', Ministry of Health & Family Welfare, Government of India: New Delhi
- ⁷³ Planning Commission of India (2011) 'Report of the working group on health research for the 12th Five Year Plan', Department of Health Research, Ministry Of Health & Family Welfare: New Delhi:
- ⁷⁴ 'The 10 burning questions on the Government Use of Patents on the four anti-cancer drugs in Thailand' http://www.moph.go.th/hot/Second_white_paper_on_the_Thai_CL_%5bEN%5d.pdf
- ⁷⁵ 'In the Supreme Court of India Civil Appellate Jurisdiction' <http://supremecourtindia.nic.in/outtoday/patent.pdf>
- ⁷⁶ 'Discoveries Leading to FDA Approval of STI571/Gleevec: Fact Sheet' <http://www.cancer.gov/newscenter/newsfromnci/2001/gleevec/timeline>
- ⁷⁷ The 10 burning questions on the Government Use of Patents on the four anti-cancer drugs in Thailand. http://www.moph.go.th/hot/Second_white_paper_on_the_Thai_CL_%5bEN%5d.pdf
- ⁷⁸ 'FDA Approval for Dasatinib' <http://www.cancer.gov/cancertopics/druginfo/fda-dasatinib>
- ⁷⁹ La revue Prescrire 'New Indication Dasatinib first line treatment for chronic myeloid leukaemia', *Prescrire International* 21(123): page number 7.
- ⁸⁰ 'Generic Sprycel Availability' <http://www.drugs.com/availability/generic-sprycel.html>
- ⁸¹ 'Research and Development Related to dasatinib (Sprycel™)' http://www.keionline.org/misc-docs/research_notes/kei_rn_2008_3.pdf
- ⁸² 'DIPP seeks details on Bristol-Myers Squibb's blood cancer drug Dasatinib' <http://www.thehindubusinessline.com/companies/dipp-seeks-details-on-bristolmyers-squibbs-blood-cancer-drug-dasatinib/article6516441.ece>
- ⁸³ BDR Pharma's application for a compulsory licence for BMS's patented cancer drug dasatinib was rejected. Ramesh Shankar, Mumbai, 31 Oct, 2013 <http://www.pharmabiz.com/NewsDetails.aspx?aid=78490&sid=1>
- ⁸⁴ IIPTA <http://www.iipta.com/ipr/blog/natco-pharma-patent-warrior-950>
- ⁸⁵ TECHNOLOGY TRANSFER: NIH-Private Sector Partnership in the Development of Taxol' <http://www.gao.gov/products/GAO-03-829>
- ⁸⁶ 'Government use licenses in Thailand: an assessment of the health and economic impacts' <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3176479/>
- ⁸⁷ 'Government use licenses in Thailand: an assessment of the health and economic impacts' <http://www.in-pharmatechnologist.com/Ingredients/Venus-to-supply-docetaxel-to-Thailand>
- ⁸⁸ Monthly Index of Medical Specialities (MIMS) India (consulted 10 December 2013).
- ⁸⁹ Brenda Waning, Warren Kaplan, Alexis C. King, Danielle A. Lawrence, Hubert G. Leufkens, and Matthew P. Fox (2009) Global strategies to reduce the price of antiretroviral medicines: evidence from transactional databases, <http://www.who.int/bulletin/volumes/87/7/08-058925/en/>

- ⁹⁰ 'What you Need to Know about Biosimilar Medicinal Products'
http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf
- ⁹¹ 'Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs)'
http://www.who.int/biologicals/areas/biological_therapeutics/BIOTHERAPEUTICS_FOR_WEB_22APRIL_2010.pdf
- ⁹² On July 18, 2013, the Biotechnology Industry Organization (BIO) submitted a letter and a 'white paper' to the USTR urging at least 12 years of market/data exclusivity in the TPP. BIO, letter, available at: <http://www.bio.org/sites/default/files/letterhead.pdf>; BIO, Trans-Pacific Partnership and Innovation in the Bioeconomy: The Need for 12 Years of Data Protection for Biologics (BIO White Paper), available at: http://www.bio.org/sites/default/files/TPP%20White%20Paper%20_2_.pdf.
- ⁹³ Brook K. Baker and K. Brook (2013) 'With One Exception Current Trade Agreements Do No Appear to Include Biologic Medicines in their Data Protection/Data Exclusivity Provisions –Implications for TPP Negotiation' 13 August 13.
- ⁹⁴ 'Cancer Medicine Prices in Low- And Middle-Income Countries' <http://www.msh.org/resources/cancer-medicine-prices-in-low-and-middle-income-countries>
- ⁹⁵ Based on the work of the Global Task Force on Expanded Access to Cancer Care and Control, Felicia M. Knaul, Julie R. Gralow, Rifat Atun, and Afsan Bhadelia (eds.) *Closing the Cancer Divide. An Equity Imperative*.
- ⁹⁶ U.S. Government National Intelligence Council (2002) *The Next Wave of HIV/AIDS: Nigeria, Ethiopia, Russia, India and China*. September, 2002.
- ⁹⁷ 'Pharma supporters ensure new drugs for cancer are not on the UN agenda'
<http://www.theguardian.com/society/sarah-boseley-global-health/2011/sep/20/cancer-pharmaceuticals-industry>
- ⁹⁸ 'For an all-party manifesto on health' <http://www.thehindu.com/opinion/op-ed/for-an-allparty-manifesto-on-health/article5797129.ece>
- ⁹⁹ 'SOUTH AFRICA: Activists protest as Novartis ruling approaches'
<http://www.irinnews.org/report/95854/south-africa-activists-protest-as-novartis-ruling-approaches>
- ¹⁰⁰ 'The 'diagonal' approach to Global Fund financing: a cure for the broader malaise of health systems?'
<http://www.globalizationandhealth.com/content/4/1/6>
- ¹⁰¹ 'Total Unaudited and Audited Global Pharmaceutical Market By Region/2012 – 2017'
http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Corporate/Press%20Room/Total_World_Pharma_Market_Topline_metrics_2012-17_regions.pdf
- ¹⁰² 'Roche Position on Access to Medicines and Diagnostics'
http://www.roche.com/de/access_to_medicines_and_diagnostics.pdf; 'Cancer Drugs Get Cheaper, in India' <http://online.wsj.com/news/articles/SB10001424052702303812904577297673910205972>;
On differential pricing for cancer drugs see 'Improving Affordability'
http://www.roche.com/responsibility/access_to_healthcare/improving_affordability.htm
- ¹⁰³ 'The importance of being earnest (and dressing the part)' <http://alexyvergara.com/2013/09/10/the-importance-of-being-earnest-and-dressing-the-part/>
- ¹⁰⁴ 'Access to medicine for patients in need: Novartis perspective'
<http://www.novartis.com/downloads/corporate-responsibility/resources/positions/access-to-medicine.pdf>
- ¹⁰⁵ 'Improving health in rural India: Commercial innovation to address health needs at the bottom of the pyramid' <http://www.novartis.com/downloads/corporate-responsibility/arogya-factsheet.pdf>
- ¹⁰⁶ Stephanie Strom, Matt Fleisher-Black (2003) 'Drug maker's vow to donate cancer medicines falls short', *New York Times*, 5 June.
<http://www.novartis.com/downloads/corporate-responsibility/resources/positions/patent-pools-pharmaceuticals.pdf>, (last accessed May 2014).
- ¹⁰⁸ 'Access to Care' http://en.sanofi.com/csr/patient/priorities/access_to_care/access_to_care.aspx
- ¹⁰⁹ 'Patents, Licensing and Technology Transfer: Working with Generic Companies and other Partners'
<http://www.bms.com/responsibility/access-to-medicines/Pages/patents-licensing-technology.aspx>
- ¹¹⁰ 'Patient Assistance Programs' <http://www.bayerpharma.com/en/corporate-responsibility/medical-care/patient-assistance-programs/index.php>
- ¹¹¹ Rohit Malpani (2004) Correspondence with author. Information based on documentation in Bayer vs. Natco case, March 2013.
- ¹¹² Marg Ewen (2014) correspondence with author. Health Action International is currently carrying out a project to map external reference pricing practices for medicines with the support of Dfid.
- ¹¹³ 'India's First Compulsory Licence Upheld, But Legal Fights Likely To Continue' <http://www.ip-watch.org/2013/03/04/indias-first-compulsory-licence-upheld-but-legal-fights-likely-to-continue/>
- ¹¹⁴ Ixabepilone is indicated in combination with another agent capecitabine for the treatment of patients with metastatic or locally advanced breast cancer resistant to treatment with an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated. Ixabepilone is indicated as monotherapy for the treatment of metastatic or locally advanced breast cancer in patients whose tumors are resistant or refractory to anthracyclines, taxanes, and capecitabine. (FDA 2007) Ixabepilone has been refused marketing authorization in the EU in 2008. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000930/smops/Negative/human_smop_000030.jsp&mid=WC0b01ac058001d127

- ¹¹⁵ 'DIPP to issue CLs for Herceptin, Dastinib & Ixabepilone – End of the line for Big Pharma's patents in the Indian market?' <http://spicyip.com/2013/01/dipp-to-issue-cls-for-herceptin.html>
- ¹¹⁶ NATCO (2012), 'NATCO granted compulsory licence for Nexavar' 12 March 2009, <http://natcopharma.co.in/index.php/news-for-dump/149-natco-granted-compulsory-licence-for-nexavar>
- ¹¹⁷ Official Journal of the Patent Office, Issue 32/2011, 12/08/2011. Publication of the Patent Office. <https://docs.google.com/viewer?a=v&pid=sites&scid=ZGVmYXVsdGRvbWFnbnxzGjIjeWlwZmlsZXN8Z3g6NDFINjAxZDlyOTY0MjMyMg>
- ¹¹⁸ 'NATCO granted compulsory licence for Nexavar' <http://natcopharma.co.in/index.php/news-for-dump/149-natco-granted-compulsory-licence-for-nexavar>
- ¹¹⁹ The Controller of Patents http://www.ipindia.nic.in/iponew/Order_30October2013.pdf
- ¹²⁰ See also: 'DIPP may seek information from DCGI to manufacture generic version of Roche's anti-cancer drug' http://articles.economicstimes.indiatimes.com/2013-08-06/news/41131672_1_compulsory-licence-trastuzumab-leena-menghaney
- ¹²¹ 'Campaign for Affordable Trastuzumab' <http://donttradeourlivesaway.files.wordpress.com/2012/10/letter-to-indian-pm-on-herceptin-for-circulation-2-october-12.pdf>
- ¹²² For a complete list of oppositions see patentoppositions.org
- ¹²³ The Patents (Amendment) Act, 2005 and The Patent (Amendment) Rules, 2006 http://cdn.patentoppositions.org/uploads/patent_office_decision/user_uploaded_file/50a63c095adc050002000004/60c87480-121d-0130-1321-1231380e54d8.pdf
- ¹²⁴ '170 Members of Congress Send Letter to Obama Criticizing India on Intellectual Property' <http://keionline.org/node/1757>
- ¹²⁵ 'US Businesses Launch Coalition For Fair Trade With India' <http://www.ip-watch.org/2013/06/18/us-businesses-launch-coalition-for-fair-trade-with-india/>
- ¹²⁶ Health Intervention and Technology Assessment Program (HITAP) (2009) Assessing the implications of Thailand's Government Use Licenses issued in 2006–2008, Bangkok: Ministry of Health.
- ¹²⁷ 'Speech by World Bank Group President Jim Yong Kim at Council on Foreign Relations: 'Count on Us'' <http://www.worldbank.org/en/news/speech/2014/04/01/speech-world-bank-group-president-jim-yong-kim-council-on-foreign-relations>
- ¹²⁸ 'Sanders Bill Would Replace Drug Monopolies with Prizes' http://www.huffingtonpost.com/james-love/sanders-bill-would-replac_b_69219.html
- ¹²⁹ The Medical Innovation Prize Fund Act: S. 1137, The Prize Fund for HIV/AIDS Act: S. 1138.
- ¹³⁰ 'Cancer Medicines and Vaccines in Developing Countries: Prizes as a Reward Mechanism for New Cancer Treatments', WORKING DOCUMENT - BARBADOS AND BOLIVIA PROPOSAL 4, http://keionline.org/misc-docs/b_b_igwg/prop4_cancer_prizes.pdf
- ¹³¹ 'Global Task Force on Expanded Access to Cancer Care and Control' <http://gtfcc.harvard.edu/icb/icb.do?keyword=k69586&tabgroupid=icb.tabgroup138264>
- ¹³² 'Push for palliative care stokes debate' <http://www.who.int/bulletin/volumes/91/12/13-021213/en/index.html>
- ¹³³ A fate that is not exclusive to cancer. See for example challenges with access to treatment of HepC. <http://www.pharmalive.com/how-much-a-battle-over-the-cost-of-the-new-hepatitis-c-drugs>
- ¹³⁴ Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries (2011) 'Closing the Cancer Divide: A Blueprint to Expand Access in Low and Middle Income Countries', Boston: Harvard Global Equity Initiative.
- ¹³⁵ 'Cancer, the New AIDS? Expanding Access to Treatment for a Silent Epidemic' <http://www.msh.org/blog/2011/11/04/cancer-the-new-aids-expanding-access-to-treatment-for-a-silent-epidemic>; 'The good news about cancer in developing countries' <http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2811%2961681-4/fulltext>; 'Global Task Force on Expanded Access to Cancer Care and Control' <http://gtfcc.harvard.edu/icb/icb.do>
- ¹³⁶ 'High-level Meeting on Non-communicable Diseases' <http://www.un.org/en/ga/president/65/issues/ncdiseases.shtml>
- ¹³⁷ Hogerzeil et al. (2013), 'Promotion of access to essential medicines for non-communicable diseases: practical implications of the UN political declaration' *The Lancet* Volume 381, No. 9867, p680–689, 23 February 2013 doi: [http://dx.doi.org/10.1016/S0140-6736\(12\)62128-X](http://dx.doi.org/10.1016/S0140-6736(12)62128-X)

Research reports

This research report was commissioned by Oxfam and written to share research results, to contribute to public debate and to invite feedback on development and humanitarian policy and practice. It does not reflect the policy positions of the publishing organizations.

For more information, or to comment on this report, email mkamalyanni@oxfam.org.uk

© Oxfam International February 2015

This publication is copyright but the text may be used free of charge for the purposes of advocacy, campaigning, education, and research, provided that the source is acknowledged in full. The copyright holder requests that all such use be registered with them for impact assessment purposes. For copying in any other circumstances, or for re-use in other publications, or for translation or adaptation, permission must be secured and a fee may be charged. E-mail policyandpractice@oxfam.org.uk.

The information in this publication is correct as of 2 May 2014.

Published by Oxfam GB for Oxfam International under ISBN 978-1-78077-804-4 in February 2015.

Oxfam GB, Oxfam House, John Smith Drive, Cowley, Oxford, OX4 2JY, UK.

OXFAM

Oxfam is an international confederation of 17 organizations networked together in more than 90 countries, as part of a global movement for change, to build a future free from the injustice of poverty. Please write to any of the agencies for further information, or visit www.oxfam.org.