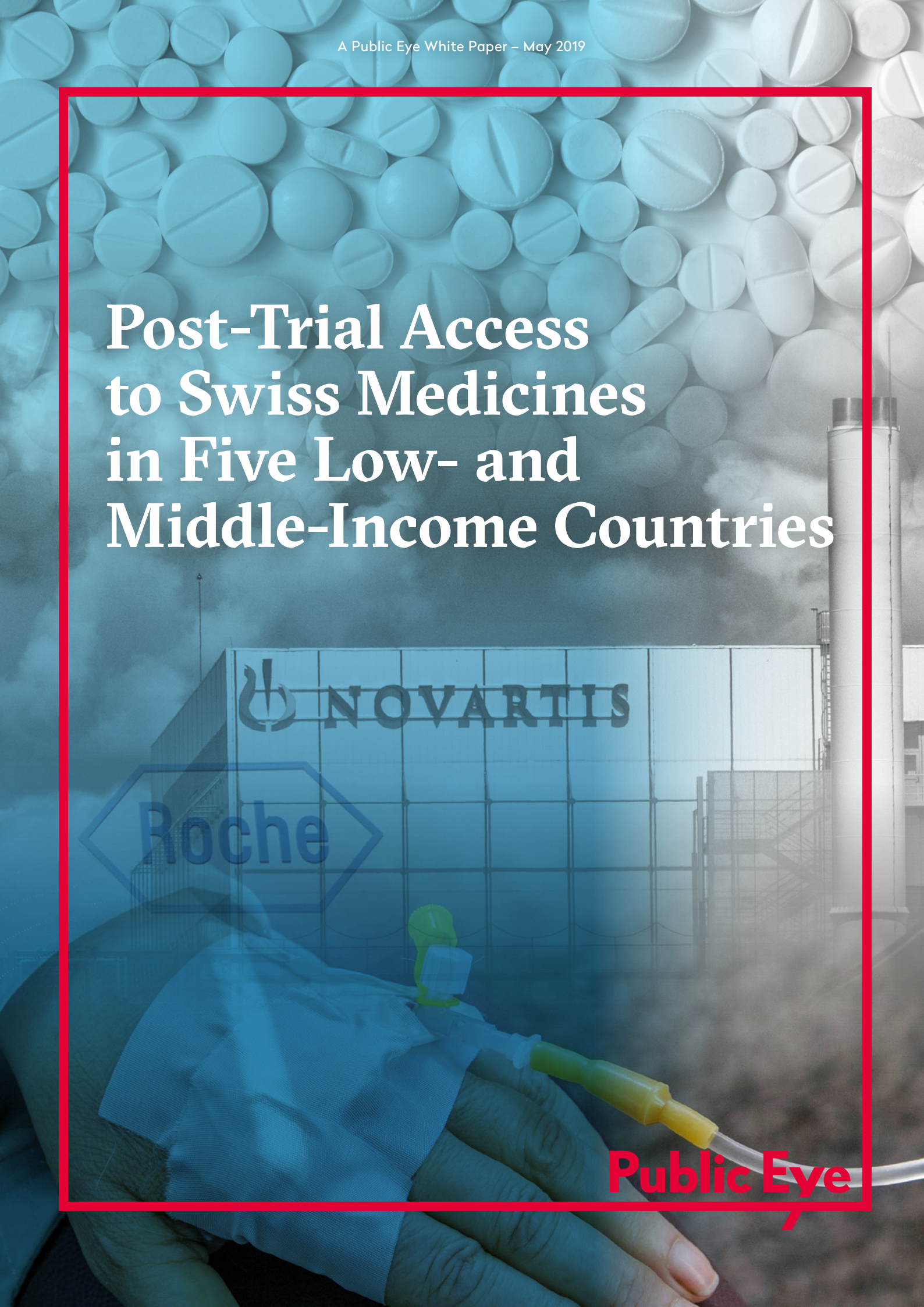
A Public Eye White Paper – May 2019

Post-Trial Access to Swiss Medicines in Five Low- and Middle-Income Countries



Public Eye

IMPRINT Post-Trial Access to Swiss Medicines in Five Low- and Middle-Income Countries. A Public Eye White Paper, May 2019, 24 pages | **Authors** Alice Kohli and Patrick Durisch | **Contribuors** Catherine Tomlinson (South Africa), Daniela Moye Holz (Mexico), Francisco Rossi (Colombia), Israel Rico-Alba (Mexico), Sergey Kondratyuk (Ukraine), Usawadee Maleewong (Thailand) | **Editor** Mary Louise Rapaud | **Layout** Karin Hutter, karinhutter.com | **Cover picture** © Roger Anis, MarkHenley/Panos, Shutterstock

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Executive Summary

The Swiss pharmaceutical firms Roche and Novartis claim to conduct clinical drug trials in low- and middle-income countries (LMICs) only when they intend to market the tested product locally. International ethical standards require vulnerable groups to benefit from the results of research carried out on them – i.e. the tested medicine should be locally accessible if proven beneficial (commonly referred to as post-trial access or PTA).

This research aims to verify whether the two Swiss pharmaceutical giants meet their ethical PTA obligation based on a selection of non-communicable diseases (NCD) medicines tested in five LMICs. Previous research shows that only 40–60% of the NCD medicines approved in high-income countries received local market approval following testing in India, South Africa and Egypt.

We selected five LMICs on different continents where both Novartis and Roche regularly conduct clinical trials: Colombia, Mexico, South Africa, Thailand and Ukraine. We identified all interventional clinical drug trials carried out and completed by both companies between 2005 and 2015 in these countries, and then shortlisted 22 NCD medicines, reflecting a balance between the companies and across different disease categories.

In terms of availability, the vast majority of the shortlisted NCD medicines were found to be approved for marketing in the selected LMIC according to the relevant national public databases: 18/18 and 20/20 in Colombia and Thailand respectively (100%), 16/17 (94%) in South Africa, 6/7 (86%) in Ukraine and 19/22 (86%) in Mexico. Even if some registrations had not been systematically renewed, as required by local regulations, the related products seemed to be available for sale to patients.

However, in terms of accessibility, registered cancer treatments remain completely unaffordable for the majority of the population if they have to pay from their own pocket. An annual breast cancer treatment with Roche's pertuzumab (brand name Perjeta), which is only available in the private healthcare sector and so not covered by basic insurance packages, costs over USD 55,000 in Mexico and in Ukraine, more than 6 and 23 times the gross national income (GNI) per capita respectively. An average worker earning the official minimum wage in these two countries would have to work for more than 30 years to pay for just one year of treatment.

Even when obtained from a public facility at a subsidised price in these two countries, an annual treatment of cancer drugs such as Roche's trastuzumab (brand name Herceptin) represents up to 15 years of working at the minimum wage if paid out-of-pocket. Although these treatments could be fully paid for by the state, it is the exception rather than the rule due to budgetary and supply constraints. While other types of shortlisted treatments (cardiovascular, diabetes, respiratory diseases) are less costly, only a handful are fully covered by basic health insurance schemes, and so can still represent a significant share of an average worker's income.

Many of the newer cancer medicines are not even included in basic health insurance packages. When they are, patients relying on free or state-subsidised treatments are lucky if they are available at the point-of-care during the whole duration of the treatment. With few exceptions, access to these medicines is simply a lottery.

Due to these inadequate pricing policies, which fail to reflect local economic realities, Novartis and Roche cannot be said to comply with their ethical obligations in terms of PTA in LMICs.

1 Introduction

1.1 – CLINICAL TRIALS IN LMICS

Clinical trials must be undertaken for a drug to be approved for marketing. Once an active substance has been discovered, synthesized and studied in the laboratory, its efficacy and safety has to be tested on humans. Companies do this in three waves of trials, which serve as the basis for the drug's authorisation. A fourth phase (usually called post-marketing studies) is sometimes undertaken for the purpose of complementary research, but this is generally less well-monitored by regulatory authorities.

Millions of people take part in tens of thousands of clinical trials at any given time. As of March 1, 2019, Roche was sponsoring almost 3500 active clinical trials in 83 countries, and Novartis almost 2700 in 82 countries.[1] In 2018, Roche spent USD 10.9 billion on research and development (R&D) while Novartis spent USD 8.5 billion.[2] The share of total R&D budgets allocated to clinical trials is not known, as the pharmaceutical industry discloses neither R&D budget details nor clinical trial costs: they are considered a trade secret. Published estimates from industry and governmental sources vary from 50% to 70% of total R&D costs spent on clinical trials.[3] However, these estimates should be taken with some caution as the methodologies and categorisations vary and the public contribution to the various development phases is usually not considered.

There has been an increased offshoring of clinical trials to developing and emerging countries over the last 20 years.

Although most clinical trials are still conducted in the United States and Europe, there has been an increased offshoring to developing and emerging countries over the last 20 years. The proportion of testing in emerging markets has grown continuously and a recent market analysis suggests it may increase even further.[4] The authors of this analysis valued the clinical trials market at USD 32 billion in 2017 and expect to register an annual growth rate of roughly 4% for their forecast period (2018–2023).

The cost of conducting clinical trials in emerging countries is estimated to be around 40–60% less than in developed countries, such as the United States, the authors of the analysis calculated. The preferred destinations for offshored, industry-sponsored clinical trials are Asia (e.g. China, India, Thailand), Eastern Europe (e.g. Russia, Ukraine, Poland), Latin America (e.g. Argentina, Brazil, Colombia, Mexico) and Africa (e.g. South Africa, Egypt). These regions also represent strong market potential for pharmaceutical multinationals.

The offshoring of clinical trials by pharmaceutical companies may result in serious ethical violations if proper safeguards for the protection of vulnerable trial participants in LMICs are not in place. Public Eye has previously conducted investigations in six countries among the favoured destinations for clinical trials: Russia, Ukraine, Argentina and India in 2013, Poland since 2015 and Egypt in 2016. The research shows that Swiss and foreign pharmaceutical multinationals take advantage of the weaknesses of local systems to accelerate drug testing and increase profits, with little regard for international ethical standards or people.[5]

1.2 – POST-TRIAL ACCESS

Much of the debate launched by NGOs and patients' organisations has centered on the ethical conduct of trials. Issues including the lack of oversight, recruitment of trial participants, reasons for their participation and informed consent-taking have been widely discussed in several recent field investigations and media reports. However, ethical issues also arise after the trials are completed.

One of the most important questions is how the trial's host country should benefit. This involves two separate issues:

a) Post-trial access to treatment for the trial participants – and possibly additional benefits to the community – until the tested product is commercially available.
b) Accessibility (i.e. availability and affordability) of the tested medicine to the general population after marketing approval has been granted.

In this study, we focused solely on the second issue. We tried to find out if marketing approval was requested by the sponsor of

the trials and if the medicines were available and accessible for the population.

According to international ethical standards, each clinical trial has to be beneficial to the population on which the medication is tested. The Council for International Organizations of Medical Sciences (CIOMS) states in its International Ethical Guidelines for Health-related Research Involving Humans: "As part of their obligation, sponsors and researchers must also make every effort, in cooperation with government and other relevant stakeholders, to make available as soon as possible any intervention or product developed, and knowledge generated, for the population or community in which the research is carried out, and to assist in building local research capacity."[6]

According to international ethical standards, each clinical trial has to be beneficial to the population on which the medication is tested.

The World Medical Association states in the Declaration of Helsinki that research on vulnerable groups – such as people in LMICs – comes with obligations: "Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research."[7]

Furthermore, the Universal Declaration on Bioethics and Human Rights by the UNESCO General Assembly states: "Benefits resulting from any scientific research and its applications should be shared with society as a whole and within the international community, in particular with developing countries."[8]

Many companies claim to comply with the above-mentioned standards. However, a drug tested in a country is not always marketed in that country. When it is marketed, the drug may be unavailable in pharmacies and/or hospitals, or its prohibitively high price makes it unaffordable for the majority of the population.

A study conducted by the Sama Resource Group for Women and Health in India in 2016 investigated the accessibility of medicines that underwent clinical trials in India. The authors found that of 167 medicines that were approved for marketing in the EU and USA, only 111 were also registered in India: an approval rate of 66.5% compared to the EU/USA.[9] The authors concluded that many multinational companies continue not to launch drugs in the LMICs where they trialled them.

A study conducted by Limaye et al. in 2014[10] compared the distribution of market application approvals between the EU/USA, India and South Africa. The results revealed that out of clinical trials with the participation of test centres in India and/or South Africa, only 60.4% clinical trials (India) and a meagre 39.9% clinical trials (South Africa) that led to market authorisation in the EU/USA had also led to a New Drug Application (NDA) approval in India or South Africa. The authors concluded that the results clearly showed that sponsors do not follow the regulations concerning marketing authorisation.

In a study conducted by Public Eye (then: Berne Declaration), Wemos, SOMO, EIPR and Shamseya about clinical trials in Egypt in 2016, the investigators could find a date for the marketing approval by the Egyptian Drug Authority (EDA) for only 15 of 24 medicines tested in the country, which corresponds to an approval rate of 62.5%. The drugs in question were all marketed in the USA and the EU.[11]

In conclusion, there has been no systematic authorisation in India, Egypt and South Africa of medicines previously tested there and proven to be beneficial, despite many sponsors claiming to comply with international ethical standards and guidelines.

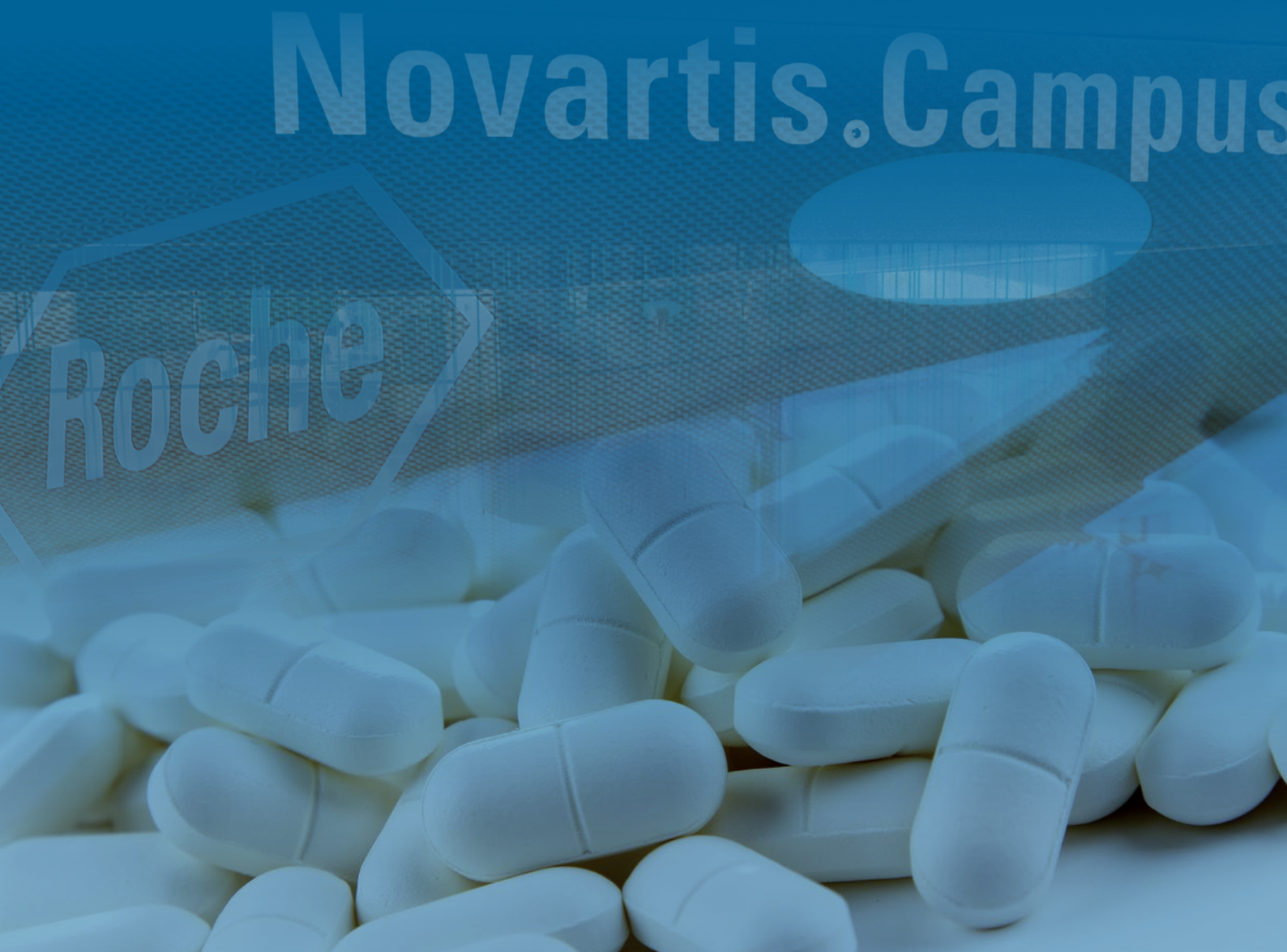
These findings contradict industry declarations. Some transnational pharmaceutical companies have long-standing, clearly written policies in place for clinical trials conducted in LMICs. And some of them even specify the need to seek market authorisation following the successful conclusion of a trial. The Swiss pharmaceutical company Roche states in its position on clinical research that "Roche intends to seek marketing authorization in all countries where we conduct clinical studies for a particular medicine or diagnostics product."[12]

Christoph Franz, Chairman of Roche, said at the 2017 annual shareholder meeting that he expects Roche to increasingly focus on research in developing and emerging countries in order to make their medicines available to the patients there. He argued that in most cases studies had to be set up on-site for regulatory reasons in order to obtain marketing authorisation for pharmaceuticals.[13] While this holds true for some jurisdictions, it does not apply to all countries. And it certainly does not explain the significant gaps between successfully concluded clinical trials and missing market authorisations, as documented above.

"Benefits resulting from any scientific research and its applications should be shared with society as a whole and within the international community, in particular with developing countries."

Novartis claims on its website: "After successful completion of clinical programs, we commit to registering our new medicines in every country where patients have participated in trials."[14] During the company's annual shareholder meeting in February 2014 and in a subsequent letter addressed to Public Eye (then: Berne Declaration), Mr Jörg Reinhardt, Chairman of Novartis, underlined that "clinical trials will only be conducted in countries where marketing approval will be requested".

2
Results



2.1 – OVERVIEW

This study aimed to answer the following questions:

1. Availability: do Swiss pharmaceutical companies systematically apply for market authorisation in the LMIC where they conduct their clinical trials?
2. Affordability: is the tested medicine, once available following registration, affordable for the general population?

In answering these questions, we aimed to find out if the communities actually benefitted from the knowledge, practices or interventions arising from the research conducted in their country, as required by international ethical standards.

We chose to focus on LMICs where both Novartis and Roche regularly conduct clinical trials (see Chart 2.1). We also wanted to spread the research across four continents, to determine if market authorisation practices are comparable globally. We therefore focused on Mexico, Colombia, South Africa, Thailand, and Ukraine.[15]

Chart 2.1 – **Clinical trials conducted by Novartis in the 5 selected countries over the period 2011–2018**[16]

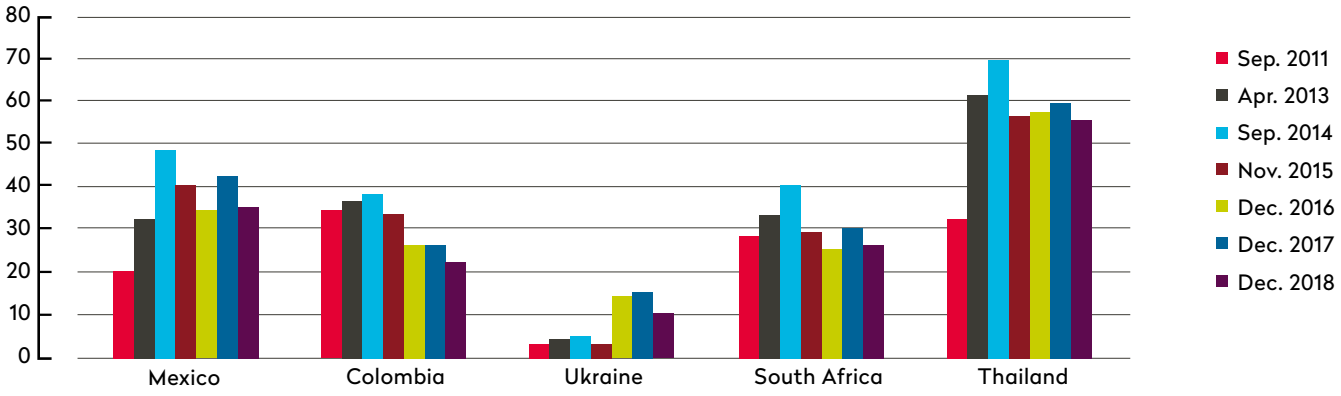
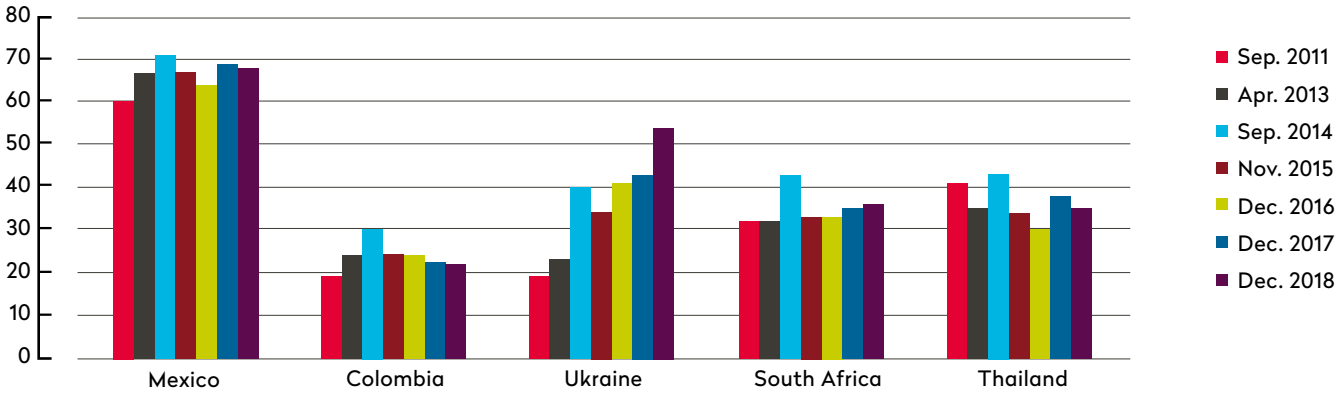


Chart 2.2 – **Clinical trials conducted by Roche in the 5 selected countries over the period 2011–2018**[17]



2.2 – AVAILABILITY

Do Swiss pharmaceutical companies systematically apply for market authorisation in the LMICs where they conduct their clinical trials? This question cannot be fully answered within the scope of this research.[18] Nevertheless, in the limited selection of five countries and 22 substances, a significant proportion of approved medicines was found (without detailing the specificities of breakdown per indication).

All of the selected products were approved for marketing in the USA and/or the EU, as they were in Colombia and Thailand (18/18 and 20/20, 100%). In South Africa and Ukraine all but one medicine were approved (16/17, 94% and 6/7, 86%).

Only in Mexico a total of three drugs within the selection were found not to have market approval, according to publicly available databases, resulting in a market approval rate of 19/22, or 86%.

Table 2.1 summarises the results on availability according to public data. It shows where the substance was part of a clinical trial completed between 2005 and 2015, and if the substance has subsequently been approved for marketing in the country.

The outcome in terms of approved medicines is better than what might have been expected based on the aforementioned studies, conducted only a few years ago. Thus, the results are encouraging. They suggest that pharmaceutical companies have listened to past criticisms from advocacy and academic groups

about the lack of registration of medicines tested in LMICs, and have become more diligent in seeking market approval in LMICs.

Mexico can be seen as an outlier, although Novartis provided some additional information that was missing on the publicly available Mexican database (see page 10). The Mexican health ministry has a specific institution to evaluate and approve medicines called COFEPRIS (Comisión Federal para la Protección contra Riesgos Sanitarios; Federal Commission for the Protection against Sanitary Risk) that has a comparable function to the Food and Drug Administration (FDA) in the USA.

In the process of market authorisation, COFEPRIS gathers all relevant evidence regarding efficacy and safety and, based on this, approves or rejects a product's registration. COFEPRIS runs an online public database ("Consulta de Registros Sanitarios") with information regarding the status of marketing approval of medicinal products.[19]

COFEPRIS was contacted about the three medicines that had been trialed in Mexico but for which no information regarding market approval was found on the database: canakinumab (brand name Ilaris), pasireotide (brand name Signifor) and ranibizumab (brand name Lucentis), all manufactured by Novartis. While the latter product appears in the COFEPRIS database, the information is incomplete e.g. there is neither mention of approved indications nor of the registration date. The investigators have asked COFEPRIS if they obtained a marketing approval request on these products, but have received no response so far to their enquiry.

A similar lack of transparency was encountered in South Africa. Medicines are registered for use in South Africa by the South African Health Products Regulatory Authority (SAHPRA) – formerly the Medicines Control Council. SAHPRA has ignored multiple requests for data for this research, and patient

Table 2.1 – **Clinical trials and subsequent market approvals**

	BRAND NAME (COMPANY)	COLOMBIA	MEXICO	SOUTH AFRICA	THAILAND	UKRAINE
1	**Avastin** (Roche)	✓	✓	✓	✓	—
2	**Herceptin** (Roche)	✓	✓	✓	✓	✓
3	**Perjeta** (Roche)	—	✓	—	✓	—
4	**MabThera (EU), Rituxan (USA)** (Roche)	✓	✓	✓	✓	✓
5	**Tarceva** (Roche)	✓	✓	✓	✓	✓
6	**Cosentyx** (Novartis)	✓	✓	✗	✓	✗
7	**Rasilez** (Novartis)	✓	✓	✓	✓	✓
8	**Utibron (USA), Ultibro Breezhaler (EU)** (Novartis)	✓	✓	✓	✓	✓
9	**Tasigna** (Novartis)	✓	✓	✓	✓	—
10	**Afinitor** (Novartis)	✓	✓	✓	✓	—
11	**RoActemra (EU), Actemra (USA)** (Roche)	✓	✓	✓	✓	—
12	**Kadcyla** (Roche)	✓	✓	—	✓	—
13	**Mircera** (Roche)	✓	✓	✓	✓	—
14	**Xeloda** (Roche)	✓	✓	✓	✓	—
15	**Entresto** (Novartis)	✓	✓	✓	✓	—
16	**Gilenya** (Novartis)	✓	✓	✓	—	—
17	**Ilaris** (Novartis)	✓	✗	✓	—	✓
18	**Signifor** (Novartis)	—	✗	✓	✓	—
19	**Zometa** (Novartis)	✓	✓	✓	✓	—
20	**Exelon** (Novartis)	—	✓	—	✓	—
21	**Galvus** (Novartis)	—	✓	—	✓	—
22	**Lucentis** (Novartis)	✓	✗	—	✓	—

— = No clinical trials completed during the considered period

groups in South Africa have reported facing the same challenges when seeking data from the regulatory body.

When confronted with the question about the status of approval of their medicines Cosentyx in South Africa and Ukraine as well as Ilaris, Signifor and Lucentis in Mexico, Novartis said that Cosentyx was approved for marketing in South Africa in September 2018, just after the deadline set for this study, although there is still no indication on the SAHPRA website. The company states that it can take up to six months before the authority publishes approval information on their website: "It appears that no updates have been provided since February 2018, resulting in the absence of information."

Novartis confirmed that Cosentyx is not approved in Ukraine. Questioned whether a marketing approval request had been submitted, the company answered that "Novartis does not discuss registration strategies for individual products".

In the case of Mexico, the company claimed that only Ilaris was not approved for marketing and Signifor as well as Lucentis were – contrary to the information we obtained from the publicly available databases at the time of the investigation. In fact, Signifor appears on a special list for orphan drugs, issued by the Mexican ministry of health.[20] Unlike in August 2018, the COFEPRIS database now[21] also contains information about the approved indications and the registration date of Lucentis. Ilaris, the company claimed, was granted a marketing authorisation in Mexico in 2013 to treat gout. However, the product is neither registered nor marketed.

2.3 – AFFORDABILITY

The data gathered from each of the five selected LMICs shows that many of the shortlisted medicines are highly priced.[22] Many are unaffordable compared to the Gross National Income (GNI) per capita and the official minimum wage for an average worker in the respective countries – especially if patients have to (co-) pay from their own pocket, which frequently happens in LMICs.

> Cancer treatments are particularly conspicuous in terms of their exorbitant prices, often leading to their exclusion from basic health package schemes in LMICs.

Cancer treatments are particularly conspicuous in terms of their exorbitant prices, often leading to their exclusion from basic health package schemes in LMICs . Even when included and paid for (partially or totally) by the state – for example, Herceptin in Mexico or South Africa – the high prices can result in cash flow problems at the point-of-care and/or frequent stock-outs, threatening accessibility throughout the duration of the treatment. Without insurance coverage, cancer treatment is simply unaffordable for many patients, particularly (but not exclusively) in LMICs. But even with insurance coverage, patients living with cancer have reported financial stress in many countries, to the extent of lowering the treatment dose, partially filling prescriptions or even foregoing treatment altogether.[23]

> Without insurance coverage, cancer treatment is simply unaffordable for many patients, particularly (but not exclusively) in LMICs.

There are three main considerations in assessing affordability. The first is the required amount of medication. Each medicine has a different standard treatment course with a specific dosage and duration. Therefore, the annual treatment cost for each medicine has to be established so as to have comparable figures of financial burden.[24]

The second consideration regards healthcare coverage, which varies considerably between countries. How many people in the country are covered by healthcare? How many people benefit from a public social security scheme and how many have to rely on private insurance? Does the insurance cover the specified medicines? If not, can the patient access them? And how much is the average out-of-pocket expenditure on medicines?

The third consideration is strongly related to the second: how much income is available to pay for the drug? In Latin America, Ojo Público compared the price of medications to the monthly minimum wage and the monthly presidential wage in each country, and the price of a car (e.g. a VW Golf).[25] In the WHO/HAI methodology,[26] the measure is the number of days the lowest paid, unskilled national government worker has to work to purchase a defined course of treatment for a specific condition.

As social insurance schemes and the capacity to pay vary considerably between the selected LMICs, we chose to answer the question of affordability through two individual country case studies: Mexico and Ukraine. The affordability analysis was based on a standard calculation of the annual treatment cost of each medicine compared with the same economic indicators (GNI per capita and official minimum wage). We also differentiated between the prices applied in the public and private healthcare sector, where relevant.[27]

These two countries are recognised as among the LMICs with the highest medicine prices and with fragmented social security schemes. Mexico is located in the backyard of the USA and Ukraine in that of the European Union (EU), both regions with among the highest drug prices in the world. Further, both Mexico (NAFTA) and Ukraine (with EFTA and the EU) have signed free trade agreements with their high-income neighbours that restrict their policy space, including in terms of medicine regulation and pricing.[28]

CASE STUDY: UKRAINE

The Ukrainian health system claims to provide universal access to unlimited care,[29] free at the point of use in public medical facilities: in reality, citizens have been facing the impoverishing consequences of health expenses for years.

Expenditure from public sources (4.4% of the GDP) covers only 57% of the services used. Furthermore, health facility expenses are dominated by fixed costs (salaries, for example, account for some 71–74% of the total), leaving little for actual service provision. This means that services are either not provided or when they are, citizens have to bear much of the costs themselves – a crippling burden on the poor who do not have adequate social protection.[30]

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Ukraine provides free or subsidised medicines in the case of outpatient treatment to certain categories of people and for certain categories of diseases (valid since 1998). Another mechanism is the reimbursement of the cost of medicines during the outpatient treatment of people suffering from cardiovascular diseases, type II diabetes, bronchial asthma (since April 1, 2017). However, none of the shortlisted medicines appear on the list of reimbursements issued by the Ukrainian Ministry of Health.

> Prices in Ukraine for the cancer medications are prohibitively high.

Table 2.2 shows the annual treatment prices of the shortlisted Roche and Novartis products that were tested between 2005 and 2015 and subsequently registered in Ukraine. The same table also compares the annual treatment costs with the GNI per capita and the minimum wage of Ukraine.

Prices in Ukraine for the cancer medications are prohibitively high. Roche's Tarceva costs a Ukrainian lung cancer patient over USD 47,000 for an annual treatment, about twenty times the gross national income per capita of the country (USD 2,390 in 2017). The price of Ilaris, a medication used to treat rheumatoid arthritis, is also surprisingly high. An annual treatment with Ilaris would cost a person earning a minimum wage the better part of their working life (25 years).

Table 2.2 – **Affordability of selected medicines tested by Roche and Novartis between 2005 and 2015 in Ukraine.**

	INN	BRAND NAME OF MEDICINE	COMPANY	DOSAGE FORM AVAILABLE	Unit reference price public procurement (USD)	Annual treatment cost (USD)	Inclusion in MoH reimbursement list for medicines	Multiple of annual minimum wage	Multiple of GNI per capita
2	**Trastuzumab**	Herceptin	Roche	440 mg Single Dose Vial	1'258.18	22'304	No	14.2	9.3
4	**Rituximab**	MabThera (EU), Rituxan (USA)	Roche	500 mg/50 ml Single Use Vial	985.80	16'147	No	10.3	6.8
5	**Erlotinib**	Tarceva	Roche	150 mg Tab	1'578.73	47'362	No	30.1	19.8
7	**Aliskiren**	Rasilez	Novartis	150 mg Tab	96.88	2'713	No	1.7	1.1
8	**Indacaterol/ Glycopyrronium**	Utibron (USA), Ultibro Breezhaler (EU)	Novartis	110/50 µg Caps	53.07	637	No	0.4	0.3
17	**Canakinumab**	Ilaris	Novartis	150 mg/6 ml Single Use Vial	2'853.63	39'951	No	25.4	16.7

CASE STUDY: MEXICO

In a survey of the affordability of medicines in Mexico, dating back to 2010, the prices of several generic and originator brand products were two to five times higher than in other Latin American countries.[31] Other studies also suggest that Mexicans are paying higher prices than people in other countries.[32] Our findings confirm this trend: of the 19 medicines for which we found pricing information in Mexico, seven had the highest price per milligram of all the surveyed countries.

> Even though many are formally insured – some even multiple times – medicines are often not reimbursed.

Understanding the affordability of the medicines in Mexico requires making sense of the Mexican health system. In 2009, a system of universal healthcare was established.[33] One important pillar of this is the people's health insurance (Seguro Popular, SP): through this insurance, the Ministry of Health provides access to health care for people who are not formally employed.[34]

In the OECD review of the Mexican health system in 2016, the authors stated that Mexico's health system persists as a cluster of distinct sub-systems, each offering different levels of care, to different groups, at different prices, with different outcomes. "Affiliation to a sub-system is not determined by need, but by a person's job. Coupled with this inequity, inefficiencies are rife. Millions of Mexicans belong to more than one insurance scheme and many millions more, when surveyed, appear not to know that they have any health insurance at all", the authors write.[35]

Out-of-pocket spending in Mexico constitutes 45% of health system revenue and 4% of household expenditure.[36] Individuals' out-of-pocket spending on health care is amongst the highest in all OECD countries. In Latin America, about 78% of all medicines are paid for out-of-pocket in retail pharmacies, a 2012 study suggests.[37] This means that even though

Table 2.3 – **Affordability of selected medicines tested between 2005 and 2015 by Roche and Novartis in Mexico.**

	INN	BRAND NAME OF MEDICINE	COMPANY	DOSAGE FORM AVAILABLE
1	**Bevacizumab**	Avastin	Roche	400 mg/16 ml Single Use Vial
2	**Trastuzumab**	Herceptin	Roche	440 mg Single Dose Vial
3	**Pertuzumab**	Perjeta	Roche	420 mg Single Use Vial
4	**Rituximab**	MabThera (EU), Rituxan (USA)	Roche	500 mg/50 ml Single Use Vial
5	**Erlotinib**	Tarceva	Roche	150 mg Tab
6	**Secukinumab**	Cosentyx	Novartis	150 mg Vial
7	**Aliskiren**	Rasilez	Novartis	150 mg Tab
8	**Indacaterol/glycopyrronium**	Utibron (USA), Ultibro Breezhaler (EU)	Novartis	110/50 µg Caps
9	**Nilotinib**	Tasigna	Novartis	200 mg Tab
10	**Everolimus**	Afinitor	Novartis	2.5 mg Tab
11	**Tocilizumab**	RoActemra (EU), Actemra (USA)	Roche	80 mg/4 ml Single Use Vial
12	**Trastuzumab-emtansine (T-DM1)**	Kadcyla	Roche	160 mg/20 ml Single Use Vial
13	**Methoxy polyethylene glycol-epoietin beta**	Mircera	Roche	30 µg Single Use Vial
15	**Sacubitril/valsartan**	Entresto	Novartis	100 mg Tab
16	**Fingolimod**	Gilenya	Novartis	0.5 mg Caps
19	**Zoledronic acid**	Zometa	Novartis	4 mg/10 ml Single Use Vial
20	**Rivastigmine**	Exelon	Novartis	1.5 mg Caps
21	**Vildagliptine**	Galvus	Novartis	50 mg Tab

many are formally insured – some even multiple times – medicines are often not reimbursed.

Table 2.3 shows the annual treatment prices of the short-listed Roche and Novartis products that were tested between 2005 and 2015 and registered in Mexico, both in the public and private healthcare sector. The same table compares the annual treatment costs with the GNI per capita and the official minimum wage of Mexico.

To be able to pay for one annual cancer treatment with any of the above-mentioned products in a private facility, a general worker earning the minimum wage in Mexico would have to work between 20 and 50 years.

Only six of the products listed in table 2.3 are covered by the basic public health insurance package for unemployed people (Seguro Popular, SP), with two of them restricted to pediatric and/or selected advanced adult cases. For affiliated SP patients, Roche's Avastin, Herceptin and Mabthera and Novartis' Ultibro, Zometa and Galvus are, in theory, free of charge, assuming the products are available at the point-of-care. If a medicine is not covered by SP, but provided in the public healthcare sector, patients might have to co-pay according to their level of income, although it is not clear by how much.[38]

The second last column of table 2.3 shows the theoretical number of years of working at the official minimum wage that would be required to pay for a product that is not covered by the health insurance; for example, the cost of cancer medications Afinitor (Novartis) and Avastin (Roche) equals 14 years of minimum wage work. This demonstrates the high societal costs of such cancer medicines, even at subsidised prices, and the financial burden such pricing policies put on national health systems.

> The cost of cancer medications Afinitor (Novartis) and Avastin (Roche) equals 14 years of minimum wage work.

Previous studies have shown that the use and access to new cancer medicines is low in Mexico, in particular due to the lack of availability in public facilities that pushes to get medicines into the private healthcare sector and paid out-of-pocket.[39]

PRIVATE HEALTH CARE SECTOR				PUBLIC HEALTH CARE SECTOR				
Unit price (USD)	Annual treatment cost (USD)	Multiple of official annual minimum wage	Multiple of GNI per capita	Unit reference price public procurement (USD)	Annual treatment cost (USD)	Free of charge through social security scheme *(Seguro Popular de Salud)*	Multiple of official annual minimum wage	Multiple of GNI per capita
1'817.53	40'554	24.5	4.7	1'051.97	23'472	**Only for children & selected adult metastatic cases**	14.2	2.7
2'373.50	42'076	25.4	4.9	1'171.98	20'776	**Yes**	12.6	2.4
3'129.66	56'334	33.8	6.5	*	56'334	**No**	34.1	6.5
2'194.03	35'938	21.7	4.2	231.59	3'793	**Only for children**	2.3	0.4
2'643.59	31'723	19.0	3.7	*	31'723	**No**	19.2	3.7
1'458.65	46'677	28.0	5.4	*	46'677	**No**	28.2	5.4
54.24	651	0.4	0.1	*	651	**No**	0.4	0.1
62.79	754	0.5	0.1	9.97	120	**Yes**	0.1	0.01
793.25	30'597	18.5	3.6	1'756.78 (120 tablets)	15'811	**No**	9.6	1.8
3'580.26	42'963	26.0	5.0	2'008.96	24'107	**No**	14.6	2.8
196.62	16'516	10.0	1.9	70.43	1'578	**No**	1.0	0.2
2'754.25	73'745	49.3	8.6	*	73'745	**No**	44.6	8.6
236.12	2'380	1.6	0.3	*	2'380	**No**	1.4	0.3
54.72	2'626	1.6	0.3	*	2'626	**No**	1.6	0.3
3'075.23	39'539	23.7	4.6	*	39'539	**No**	23.9	4.6
321.08	3'853	2.3	0.4	3.34	40	**Yes**	0.02	0.005
117.25	1'407	0.8	0.2	*	1'407	**No**	0.9	0.2
21.19	545	0.3	0.1	5.24	135	**Yes**	0.1	0.02

* *Not officially listed, private price applies*

3 Conclusion

Vulnerable groups should benefit from the knowledge, practices and interventions that result from the medical research they participated in,[40] and the benefits from the scientific research should be shared with society as a whole and within the international community, in particular with developing countries.[41] While the ethical guidelines are clear, we have shown that pharmaceutical companies often take only the smallest step possible to benefit the communities on which they have conducted clinical research.

The results regarding the availability of medicines tested in LMICs appear to show an improvement in comparison to previous similar PTA studies. We found that between 86% and 100% of all the medicines selected for this study have been approved in the selected countries. This may be partially explained by the fact that the selected countries are, for multinational pharmaceutical companies such as Novartis and Roche, interesting emerging markets for their highly priced medicines, despite the limited number of patients who can afford to pay. It may also suggest that Novartis and Roche have listened to past criticisms from advocacy groups and have become more diligent in seeking market approval following testing of their drug candidates, at least in the five LMICs selected for this research.

> "It amazes me that they have done all these clinical trials in Thailand – while some of the products are totally unaffordable for most of the people here."

The 100% result in Colombia may also be linked to developments in the country's pharmaceutical policy over the last decade. Even if a patented medicine is not included in the Colombian health benefits scheme (Plan Obligatorio de Salud, or POS) because of its high price, legal avenues can be pursued to have the drug covered by the national health system, and hence paid for from the public purse. This may provide an additional incentive to seek marketing approval in the increasingly important Colombian pharmaceutical market. Between 2003 and 2009, reimbursements for highly priced medicines not covered by the POS grew on average by 70% per year, reaching over USD 1.3 million in 2010.[42]

The question of whether both Swiss companies systematically apply for market authorisation in all the LMICs where they test their medicines cannot be answered by the limited scope of this study; this would require further research in other LMICs and over different time periods.

Regardless, the dark side of the issue is affordability. When confronted with the selection of medicines, Giten Khwairakpam, a health policy expert from Thailand, said: "It amazes me that they have done all these clinical trials in Thailand – while some of the products are totally unaffordable for most of the people here."

Generally the various cancer treatments are officially priced far above the gross national income (GNI) per capita, requiring decades of working at the official minimum wage to pay for just one year of treatment. Many of the newer cancer medicines are not included in basic health insurance packages, and if they are, patients reliant on free or state-subsidised healthcare are lucky to find them at the point-of-care. With few exceptions, access to these medicines is simply a lottery.

Novartis and Roche cannot claim to comply with their ethical obligations in terms of PTA in LMICs due to their pricing policies, which do not adequately consider the economic circumstances of vulnerable households. In particular, economically vulnerable patients living in LMICs where Novartis and Roche test their medicines are not benefitting from therapeutic progress and too often have to rely on older, less efficacious treatments, despite having contributed to the development of newer therapies through their participation in clinical trials. This is a breach of the ethical principles laid down in the Declaration of Helsinki, which both Roche and Novartis publicly claim to follow scrupulously. The Swiss pharma giants must make significantly greater efforts in their pricing policy to ensure that products of therapeutic value are systematically both available (market approval) and accessible to the entire population in the countries where they are tested.

4
Recommendations

PHARMACEUTICAL COMPANIES SHOULD:

- not conduct clinical drug trials in LMICs where they have no intention of marketing the tested medicines;
- continue to systematically apply for market authorisation for the products tested in LMICs whose results have proven beneficial (added therapeutic value);
- show increased due diligence in adopting pricing policies that take into account the income and insurance situation of the population of each country separately, including economically vulnerable groups;
- adopt and make public clear internal PTA policies that are fully compliant with the Declaration of Helsinki and other relevant international ethical guidelines addressing the situation of vulnerable groups in LMICs.

THE SWISS AGENCY FOR THERAPEUTIC PRODUCTS (SWISSMEDIC) SHOULD, AS A MEMBER OF THE INTERNATIONAL COUNCIL ON HARMONISATION (ICH):

- suggest and advocate for a revision to the ICH Guidelines for Good Clinical Practice (ICH-GCP) to include a section on PTA (currently non-existent). As these GCP serve as a catalogue of procedures for the proper conduct of clinical trials, this inclusion would induce sponsors and investigators to develop and make public future PTA provisions in the relevant LMICs.

REGULATORY AUTHORITIES IN LMICS SHOULD:

- improve their transparency regarding market authorisation processes, not only for medicines that have been granted approval but also for those that are under examination (pending applications). This would help to determine if companies are proactively seeking registration of all the products they have been testing in the respective LMICs;
- make all pricing and procurement data freely and easily available, be it via national tenders or directly at public healthcare facilities and/or the provincial level, so that the public can assess and monitor medicine availability and affordability in the public sector.

Annex 1
Methodology

This study aimed to answer the following questions:

1. Availability: do Swiss pharmaceutical companies systematically apply for market authorisation in the LMIC where they conduct their clinical trials?
2. Affordability: is the tested medicine, once available following registration, affordable for the general population?

In answering these questions, we aimed to find out if the communities actually benefitted from the knowledge, practices or interventions resulting from the research conducted in their country, as required by international ethical guidelines.

Selection of focus countries

The focus of the study lay on LMICs in which both Novartis and Roche regularly conduct clinical trials (see charts 2.1 and 2.2). We also wanted to spread the research across four continents and different disease categories to determine if market authorisation practices are comparable globally. For these reasons we focused on Mexico, Colombia, South Africa, Thailand, and Ukraine.

Selection of trials

Interventional trials sponsord by Novartis and Roche completed between 2005 to 2015 were selected. Based on previous studies we decided that 30 months was an adequate period of time for the sponsor to file a New Drug Application in the respective country.[43]

From the selection of completed trials, a shortlist was established of 22 medicinal products tested in at least one of the selected countries, taking into account both:

- a balance between Roche and Novartis products, and
- medicines across different disease categories.

The Declaration of Helsinki requires that every clinical trial be registered in a publicly accessible database before recruitment of the first trial participant.[44] The source used to collate details of clinical trials is the United States National Library of Medicine database,[45] recognised as a primary register by the World Health Organization (WHO). It is one of the most comprehensive global trial registries, where data can be obtained freely and easily.

Search criteria in the 'advanced search' field were: 'completed', 'interventional studies' and 'industry sponsored'. The search was restricted to trials sponsored by Novartis and Hoffmann-La Roche or Genentech (in 'search terms'), and to the focus countries (in 'country 1'). Trials conducted between 2005 and 2015 were selected manually from the search results (the 'first received' and 'last updated' fields in the search engine proved not helpful for the research).

Data on market approval in high-income countries

The databases used by Public Eye to study the comparative approval status of drugs in the USA, the EU and Switzerland were from the US Food and Drug Administration (US FDA),[46] the European Medical Agency (EMA),[47] and the Swiss medical agency Swissmedic.[48]

Data on treatment dosage

To establish the recommended standard treatment dosage and the number of milligrams needed for an annual therapy for the medicines in question, we consulted the Swiss Compendium of Medicines[49] and the German Federal Joint Committee websites[50].

Data on market approval, prices and affordability

To establish the status of market approval as well as the prices of the medicines listed above – and in the selected cases of Mexico and Ukraine, their affordability – we consulted different sources for each country.

COLOMBIA

Public Eye used the online database of the National Institute for Surveillance of Medicines and Food (Instituto Nacional de Vigilancia de Medicamentos y Alimentos, Invima) to study the approval status of drugs in Colombia.[51] We obtained the unit prices from sources at the Colombian Ministry of Health[52] and from the private information platform Med-Informatica[53]. We used the conversion rate on August 31, 2018 given by the Oanda currency converter.[54]

MEXICO

To study the approval status of drugs in Mexico, Public Eye used the registry provided by Mexico's drug authority. COFEPRIS runs a public online database ('Consulta de Registros Sanitarios') with information regarding the status of marketing approval of medicinal products.[55]

To obtain the maximum selling price for patented medicines in private healthcare facilities, we used the official list established by the Mexican Ministry of Economy.[56] The unit price in private pharmacies was obtained from the online pharmacy Farmacia San Pablo.[57] When there were two different unit prices in local currency (MXN), we chose the cheapest one for the calculation of the unit price in USD.

With this unit pricing data and the above-mentioned dosage/treatment cycles data from the Swiss Compendium and the German Federal Joint Committee, we obtained the annual treatment cost in USD for the private sector for a 70 kg/170 cm patient with 1.82 m² body surface.

For public healthcare facilities, we obtained the unit reference price valid in the public sector via the guidelines for procurement published by the Mexican Secretary of Health[58] or, when missing, the guidelines for procurement published by the Instituto Mexicano del Seguro Social (IMSS),[59] one of the public health insurances. We established the possibility of a state reimbursement for each treatment by consulting the Cuadro Básico y Catálogo de Medicamentos of the Consejo de Salubridad General.[60] We also checked if any of the medications could potentially be passed on to patients free of charge via the Catálogo Universal de Servicios de Salud (CAUSES),[61] as well as via the list of illnesses that are known to cause exorbitant costs (Lista enfermedades que ocasionan gastos catastróficos).[62]

We used the same calculation method as above to obtain the annual treatment costs using the unit price in USD valid for the public healthcare sector (where available).

Using the 2018 minimum wage for a general worker (MXN 88.36 or USD 4.6 per day)[63] we calculated the number of years this person would have to work to pay for one year of treatment with the pharmaceutical products in question, both in private or public healthcare facilities. We also compared the annual treatment cost in both sectors with the gross national income (GNI) per capita as provided by the World Bank.[64]

For all conversions from MXN to USD we used the average rate on August 31, 2018 given by the Oanda currency converter.[65]

SOUTH AFRICA

Public Eye used the monthly registration notifications of medicines to study the approval status of drugs in South Africa. The South African Health Products Regulatory Authority (SAHPRA, formerly Medicines Control Council, MCC) publishes the notifications as PDF files on their website.[66]

All single exit prices are publicly available on the Medicine Price Registry, a joint project of the Department of Health and Open Up, an organisation advocating for an open data strategy in South Africa.[67] We used the conversion rate on August 31, 2018 given by the Oanda currency converter.[68]

SWITZERLAND

We obtained the Swiss prices (which we use as a reference for the list in Annex 3) from the List of Specialties (LS) archive of 2018 prices available on the home page of the LS database.[69] Only prices valid as at September 1, 2018 were considered. Both the ex-factory and the public (list) price are displayed for each product/packaging. We used the conversion rate on August 31, 2018 given by the Oanda currency converter.[70]

THAILAND

Public Eye used the online database of the Thailand Food and Drug Administration[71] to study the approval status of drugs in Thailand. For the registration date and the status of the registration processes, we consulted FDA staff directly. We obtained the drug purchasing prices of public hospitals from the Drug and Medical Supply Information Center (DMSIC), Ministry of Public Health.[72] We used the conversion rate on August 31, 2018 given by the Oanda currency converter.[73]

UKRAINE

Data on marketing authorisations was obtained using the online version of the State Register of Medicinal Products of Ukraine maintained by State Expert Center of the Ministry of Health of Ukraine.[74]

We consulted various databases to establish the affordability of the medicines. To obtain the unit prices in local currency (UAH), we used the information provided by the Ukrainian State Register of Medicines[75] and from the ProZorro Public Procurement database.[76] Pharmacy prices were obtained from an independent database on available products in Ukraine[77] as well as from direct calls to pharmacies. We used the conversion rate on August 31, 2018 given by the Oanda currency converter.[78]

With this unit pricing data and the above-mentioned dosage/treatment cycles data from the Swiss Compendium and the German Federal Joint Committee, we obtained the annual treatment cost in USD.

To determine whether a medicine could potentially be subsidised by the State, we consulted the 2018 version of the government reimbursement programme, administered by the National Health Service of Ukraine.[79] None of the shortlisted molecules is actually included in the reimbursement list of medicines in Ukraine. However, hospitals and the Ministry of Health can procure them through state funds, depending on need, which is (re)defined on an annual basis.

Using the 2018 minimum wage for an average worker (UAH 3'723 or USD 131.2 per month)[80] we calculated the number of years this person would have to work to pay for one year of treatment with the pharmaceutical products in question. We also compared the annual treatment cost in both sectors with the gross national income (GNI) per capita as provided by the World Bank.[81]

TIMELINE

Once Public Eye established the inventory of clinical trials conducted in the respective countries, based on the criteria mentioned in the previous sections, local researchers were mandated to investigate if and when the medicines were approved for marketing in their country. They also sought information about the prices of the medicines and gathered information on the health insurance system in their country.

The study started in July 2018; the results by local researchers on market authorisation were gathered by September 1, 2018; the prices were investigated in August 2018, and conversed to USD at the then applicable exchange rate.

The affordability case studies were conducted after the market authorisation data was obtained.

Annex 2

List of medicines tested between 2005 and 2015 in one or more selected LMIC

	BRAND NAME	INTERNATIONAL NON-PROPRIETARY NAME (INN)	COMPANY	DISEASE CATEGORY (INDICATIONS)	CLINICAL TRIALS CONDUCTED IN
1	**Avastin**	Bevacizumab	Roche	Cancer (lung, breast, colorectal, etc.)	*All countries but Ukraine (completed 2016)*
2	**Herceptin**	Trastuzumab	Roche	Cancer (breast)	*All 5 countries*
3	**Perjeta**	Pertuzumab	Roche	Cancer (breast)	*All, but only completed in Mexico & Thailand during considered period*
4	**MabThera (EU), Rituxan (USA)**	Rituximab	Roche	Cancer (leukemia), Immune disorders (rheumatoid arthritis)	*All 5 countries*
5	**Tarceva**	Erlotinib	Roche	Cancer (lung, pancreas)	*All 5 countries*
6	**Cosentyx**	Secukinumab	Novartis	Skin (psoriasis), Multiple sclerosis, Immune disorders	*All 5 countries*
7	**Rasilez (EU), USA: not registered**	Aliskiren	Novartis	Cardiovascular disorders (heart, hypertension)	*All 5 countries*
8	**Utibron (USA), Ultibro Breezhaler (EU)**	Indacaterol/ Glycopyrronium	Novartis	Respiratory disorders (asthma, COPD)	*All 5 countries*
9	**Tasigna**	Nilotinib	Novartis	Cancer (leukemia, gastrointestinal)	*All countries but Ukraine (no trials)*
10	**Afinitor**	Everolimus	Novartis	Cancer (various types), Immunosuppressant (transplant)	*All countries but Ukraine (no trials)*
11	**RoActemra (EU), Actemra (USA)**	Tocilizumab	Roche	Immune disorders (rheumatoid arthritis)	*All countries but Ukraine (no trials)*
12	**Kadcyla**	Trastuzumab-Emtansine (T-DM1)	Roche	Cancer (breast)	*All countries but South Africa & Ukraine (to be completed 2023/24)*
13	**Mircera**	Methoxy Polyethylene glycol-Epoietin Beta	Roche	Cardiovascular disorder (anemia)	*All countries but Ukraine (completed 2016)*
14	**Xeloda**	Capecitabine	Roche	Cancer (breast, colorectal, gastric, liver, etc.)	*All countries but Ukraine (completed 2016)*
15	**Entresto**	Sacubitril/Valsartan	Novartis	Cardiovascular disorder (heart, hypertension)	*All countries but Ukraine (no trials)*
16	**Gilenya**	Fingolimod	Novartis	Nervous system (Multiple sclerosis)	*All countries but Thailand & Ukraine (no trials)*
17	**Ilaris**	Canakinumab	Novartis	Metabolic (diabetes), immune disorders (arthritis)	*All countries but Thailand (no trials)*
18	**Signifor**	Pasireotide	Novartis	Metabolic (hormonal disorder), cancer (neuroendocrine)	*All countries but Ukraine (no trials) & Colombia (completed 2016)*
19	**Zometa**	Zoledronic Acid	Novartis	Metabolic (hormonal disorder), Cancer (hormone sensitive)	*All countries but Ukraine (no trials)*
20	**Exelon**	Rivastigmine	Novartis	Nervous system disorder (Alzheimer)	*Mexico and Thailand*
21	**Galvus**	Vildagliptine	Novartis	Metabolic (diabetes)	*All but Ukraine (no trials), Colombia & South Africa (completed 2019)*
22	**Lucentis**	Ranibizumab	Novartis	Ophtalmologic disorder (age-related macular degeneration)	*All countries but Ukraine & South Africa (no trials)*

Annex 3

Overview of unit prices of selected medicines in all countries

Affordability of selected medicines tested between 2005 and 2015 by Roche and Novartis in Mexico

	INN	COMPANY	BRAND NAME	UNIT PRICE COLOMBIA (USD)	UNIT PRICE MEXICO (USD)
1	**Bevacizumab**	Roche	Avastin	1'316.31 (400 mg/16 ml vial)	1'817.53 (400 mg/16 ml vial)
2	**Trastuzumab**	Roche	Herceptin	1'623.27 (440 mg vial)	2'373.50 (440 mg vial)
3	**Pertuzumab**	Roche	Perjeta	2'517.53 (420 mg vial)	3'129.66 (420 mg vial)
4	**Rituximab**	Roche	MabThera (EU) Rituxan (USA)	1'277.23 (500 mg/50 ml vial)	2'194.03 (500 mg/50 ml vial)
5	**Erlotinib**	Roche	Tarceva	1'977.13 (30 × 150 mg tablets)	2'643.59 (30 × 150 mg tablets)
6	**Secukinumab**	Novartis	Cosentyx	1'276.52 (150 mg/ml vial)	1'458.65 (150 mg/ml vial)
7	**Aliskiren**	Novartis	Rasilez (EU), USA: Not registered	29.85 (30x150 mg tablets)	54.24 (28 × 150 mg tablets)
8	**Indacaterol/ Glycopyrronium**	Novartis	Utibron (USA), Ultibro Breezhaler (EU)	40.46 (143 mg/63 mg inhaler)	62.79 (30 × 110/50µg caps)
9	**Nilotinib**	Novartis	Tasigna	1'049.93 (40 × 250 mg tablets)	793.25 (28 × 200 mg tablets)
10	**Everolimus**	Novartis	Afinitor	4'577.14 (30 × 10 mg tablets)	3'580.26 (30 × 10 mg tablets)
11	**Tocilizumab**	Roche	RoActemra (EU) Actemra (USA)	103.30 (80 mg vial)	196.62 (80 mg vial)
12	**Trastuzumab-Emtansine (T-DM1)**	Roche	Kadcyla	2'870.11 (160 mg vial)	2'754.25 (160 mg vial)
13	**Methoxy Polyethylene Glycol-Epoietin Beta**	Roche	Mircera	140.34 (100 µg vial)	236.12 (100 µg vial)
14	**Capecitabine**	Roche	Xeloda	217.60 (120 × 500 mg tablets)	*Price not determined*
15	**Sacubitril/Valsartan**	Novartis	Entresto	87.52 (60 × 100 mg tablets)	54.72 (30 × 100 mg tablets)
16	**Fingolimod**	Novartis	Gilenya	441.13 (7 × 0.5 mg caps)	3'075.23 (28 × 0.5 mg caps)
17	**Canakinumab**	Novartis	Ilaris	12'067.59 (150 mg vial)	*Not registered in Mexico*
18	**Pasireotide**	Novartis	Signifor	2'265.51 (40 mg vial)	*Registered as orphan drug*
19	**Zoledronic Acid**	Novartis	Zometa	147.86 (4 mg vial)	321.08 (4 mg vial)
20	**Rivastigmine**	Novartis	Exelon	648.46 (100 × 36 mg patches)	117.25 (30 × 18 mg patches)
21	**Vildagliptine**	Novartis	Galvus	16.47 (28 × 25 mg tablets)	21.19 (28 × 50 mg tablets)
22	**Ranibizumab**	Novartis	Lucentis	3'380.34 (10 mg vial)	1'015.73 (10 mg vial)

UNIT PRICE SOUTH AFRICA (USD)	UNIT PRICE THAILAND (USD)	UNIT PRICE UKRAINE (USD)	UNIT EX-FACTORY PRICE SWITZERLAND (USD)	UNIT PUBLIC (LIST) PRICE SWITZERLAND (USD)
1'227.37 (400 mg/16 ml vial)	554.98 (100 mg/4 ml vial)	914.02 (400 mg/16 ml vial)	1'350.48 (400 mg/16 ml vial)	1'544.53 (400 mg/16 ml vial)
1'628.40 (440 mg vial)	1'372.95 (440 mg vial)	1'258.18 (440 mg vial)	1'910.94 (440 mg vial)	2'159.22 (440 mg vial)
Not registered in South Africa	3'049.11 (420 mg vial)	3'110.56 (420 mg vial)	3'074.77 (420 mg vial)	3'405.14 (420 mg vial)
1'162.60 (500 mg/50 ml vial)	1'844.48 (500 mg/50 ml vial)	985.80 (500 mg/50 ml vial)	1'458.60 (500 mg/50 ml vial)	1'663.10 (500 mg/50 ml vial)
1'811.59 (30 × 150 mg tablets)	1'813.63 (30 × 150 mg tablets)	1'578.73 (30 × 150 mg tablets)	2'578.78 (30 × 150 mg tablets)	2'891.65 (30 × 150 mg tablets)
Not registered in South Africa	*No data from public hospital*	*Not registered in Ukraine*	695.73 (150 mg/ml vial)	805.30 (150 mg/ml vial)
Registered as Tekturna, but not marketed in South Africa	24.10 (28 × 150 mg tablets)	96.88 (28 × 150 mg tablets)	*No official data available (LS)*	*No official data available (LS)*
33.20 (30 × 110/50 µg caps)	44.23 (30 × 110/50µg caps)	53.07 (30 × 110/50µg caps)	50.15 (30 × 110/50 µg caps)	74.46 (30 × 110/50 µg caps)
1'902.74 (112 × 200 mg tablets)	1'065.22 (28 × 200 mg tablets)	*Price not determined*	1'644.15 (28 × 200 mg tablets)	1'866.59 (28 × 200 mg tablets)
2'253.57 (30 × 10 mg tablets)	1'523.41 (30 × 10 mg tablets)	*Price not determined*	3'832.91 (30 × 10 mg tablets)	4'182.25 (30 × 10 mg tablets)
80.09 (80 mg vial)	205.67 (80 mg vial)	*Price not determined*	173.11 (80 mg vial)	215.65 (80 mg vial)
Not registered in South Africa	2'121.97 (160 mg vial)	3'172.09 (160 mg vial)	2'848.71 (160 mg vial)	3'173.46 (160 mg vial)
131.31 (100 µg vial)	*No data from public hospital*	78.23 (100 µg vial)	257.59 (100 µg vial)	312.63 (100 µg vial)
260.69 (120 × 500 mg tablets)	461.22 (120 × 500 mg tablets)	*Price not determined*	262.22 (120 × 500 mg tablets)	317.93 (120 × 500 mg tablets)
50.67 (28 × 100 mg tablets)	*No data from public hospital*	*Price not determined*	143.33 (56 × 100 mg tablets)	181.43 (56 × 100 mg tablets)
795.05 (28 × 0.5 mg caps)	*Not registered in Thailand*	*Price not determined*	1'875.66 (28 × 0.5 mg caps)	2'120.52 (28 × 0.5 mg caps)
Registered, but not marketed in South Africa	*Not registered in Thailand*	2'853.63 (150 mg vial)	12'204.09 (150 mg vial)	12'762.70 (150 mg vial)
2'221.08 (60 × 0.3 mg vials)	*No data from public hospital*	*Price not determined*	2'075.42 (30 × 0.3 mg vials)	2'339.62 (30 × 0.3mg vials)
90.04 (4 mg vial)	377.06 (4 mg vial)	*Price not determined*	175.84 (4 mg vial)	218.74 (4 mg vial)
98.90 (56 × 4.5 mg caps)	118.83 (56 × 1.5 mg caps)	*Price not determined*	91.00 (56 × 4.5 mg caps)	121.35 (56 × 4.5 mg caps)
11.36 (28 × 50 mg tablets)	*No data from public hospital*	*Price not determined*	20.56 (28 × 50 mg tablets)	40.50 (28 × 50 mg tablets)
532.57 (10 mg vial)	1'387.63 (10 mg vial)	*Price not determined*	944.89 (2.3 mg/0.23 ml vial)	1'099.68 (2.3 mg/0.23 ml vial)

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International ethical standards require vulnerable groups to benefit from the results of research carried out on them – i. e. the tested drugs should be locally available and accessible if proven beneficial. This new Public Eye research aimed to verify whether Swiss pharmaceutical firms Roche and Novartis meet their ethical obligations regarding post-trial access (PTA) to 22 non-communicable diseases (NCD) medicines tested in Colombia, Mexico, South Africa, Thailand and Ukraine.

If the results regarding availability of medicines (local marketing approval) have improved in comparison to previous similar studies, the dark side of the issue is affordability. Only a handful of the Swiss NCD drugs are fully covered by basic insurance schemes allowing for free or state-subsidised healthcare e. g. in Mexico or Ukraine. Various cancer treatments are priced far above the gross national income per capita, requiring decades of working at the official minimum wage to pay for just one year of treatment. With few exceptions, access to these medicines is simply a lottery.

Novartis and Roche cannot claim to comply with their ethical PTA obligations in low- and middle-income countries due to their inadequate pricing policies, which fail to reflect local economic realities.

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