



Teaching Experience: Inequalities in the Access to Medication to Fight against Covid-19

Cristina Vilaplana-Prieto¹

University of Murcia, Spain¹

Abstract

This teaching experience studies the market for 8 pharmaceutical products used to fight the pandemic (remdesivir, favipiravir, lopinavir/ritonavir, chloroquine, hydroxychloroquine, sofosbuvir, pirfenidone and tocilizumab) in 13 countries (Bangladesh, Brazil, China, Egypt, France, India, Malaysia, Pakistan, South Africa, Sweden, Turkey, United Kingdom and United States). Through the analysis of prices and costs, we reflect on the difficulty of access to treatment according to the country.

Keywords: *patents, Covid-19, pharmaceutical products, mark-up, costs.*

1. Introduction

As the Sars-CoV2 pandemic continues to grow, researchers around the world are urgently seeking new treatments to prevent infection, cure those infected, or lessen the severity of the disease. As of 30th March 2021, 128.3 million cases have been confirmed and 1.9 million people have died. Although there are several recently approved vaccines, clinical trials are underway to "re-use" drugs normally indicated for other diseases [1]. The shorter development time and reduced costs of using existing compounds are particularly advantageous compared to the discovery of new drugs in a pandemic situation, where time is of the essence.

Antiviral drugs include the nucleotide analogue remdesivir, which was previously used experimentally but without success against Ebola [2], favipiravir, used to treat influenza [3], the HIV protease inhibitor lopinavir/ritonavir [4], the antimalarials chloroquine and hydroxychloroquine [5], and the direct-acting antivirals sofosbuvir and daclatasvir [6] (IRCT, 2020). In addition, treatments to improve lung function and reduce inflammation, such as pirfenidone [7] and tocilizumab [8], are being evaluated in clinical trials. This educational project is designed for students in Economics, Business Administration, Political Science and Sociology. The objective is to deepen knowledge of the pharmaceutical market: (i) to demonstrate in a tangible way the differences between production costs and final prices of medicines, (ii) to perceive the difficulty of access to certain treatments depending on the country, (iii) to reflect on what initiatives should be implemented in an international emergency context such as the one we are experiencing. This will be done by consulting statistical bases and reading support documents on the structure of the pharmaceutical market. It is best to carry out this practice in small groups and then share it in order to favour "withing groups" and "between groups" interactions.

2. Metodology

2.1. Preparation of price and cost information

The minimum production costs of medicines can be estimated by calculating the cost of active pharmaceutical ingredients, which is combined with the costs of excipients, formulation, packaging and a profit margin to estimate the price of the 'finished product', i.e. the ready-to-use medicine [9]. Table 1 shows, for each drug, the duration of treatment and the number of doses to be administered each day, the daily cost of treatment and the total cost.

Table 1. Characteristics of each drug. Daily cost and total cost

	Length of the treatment	Daily doses	Total treatment cost (\$)	Daily cost (\$)
Remdesivir	10 days	2 the 1st day; 1 other days	9	0.93
Favipiravir	14 days	2 per day	20	1.45
Lopinavir	14 days	2 per day	4	0.28
Hidroxicloroquine	14 days	1 per day	1	0.08
Cloroquine	14 days	1 per day	0.3	0.02
Azitromicine	14 days	1 per day	1.4	0.2
Sofosvubir	14 days	1 per day	5	0.39
Pirfenidone	28 days	3 per day	31	1.09
Tocilizumab	-	2	177.5	355



Source: Own work using data from [10]. For Tocilizumab the table has been completed using information from [Table 1, Cost-Comparison Table for Biologic Disease-Modifying Drugs for Rheumatoid Arthritis - Tocilizumab \(Actemra\) - NCBI Bookshelf \(nih.gov\)](#)

Price information was obtained through published lists for each medicine, although all the medicines analysed in this study are available in the selected countries. Where more than one price was available for the same medicine, the lowest price was chosen. Table 2 shows the price of full treatment for each drug and country.

Table 2. Price for complete Covid-19 treatment (\$)

	Remdesivir	Favipiravir	Lopinavir	Hidroxicloroquine	Cloroquine	Azithromicine	Sofosvubir	Pirfenidone	Tocilizumab
Bangladesh	600	-	-	3	0,2	5	168	124	690
Brazil	600	-	-	-	-	19	4289	-	-
China	600	231	17	19	5	7	-	1379	1.950
Egypt	600	-	-	-	-	-	-	-	606
United States	3.120	-	503	18	93	63	18610	9.606	3.383
France	2.340	-	97	5	-	44	-	2.344	-
India	600	112,8	40	2	1	5	7	100	806
Malasya	600	-	-	7	2	11	-	-	-
Pakistan	600	-	-	-	-	-	6	-	510
United Kingdom	2.340	-	144	4	8	11	7832	2.561	914
South Africa	600	-	15	-	5	35	-	2.490	566
Sweden	2.340	-	172	3	4	16	-	2.196	-
Turkey	600	-	149	3	-	-	-	1.499	650

Source: Own work using data from [10]. For remdesivir and favipiravir, information has been completed using [Remdesivir developed country price announced | Medicines Law & Policy \(medicineslawandpolicy.org\)](#) y [India's Glenmark cuts price of COVID-19 drug favipiravir version to \\$1 per tablet | Reuters](#). Price for treatment with remdesivir was 600\$ in developing countries, 2.340\$ in developed countries and 3.120 in United States.

2.2. Content of the practice

The practice begins with the reading of [11] and [12], both available on the internet. After this reading, the following introductory questions are posed:

- What special characteristics differentiate medicines from other goods?
- What type of market do you consider to be the pharmaceutical market?
- Does it share characteristics with a market of perfect competition? Given your answer to this question, do you consider that there may be a market failure in the pharmaceutical market?
- What are the advantages and disadvantages of pharmaceutical patents?
- Do you consider that the knowledge on which new pharmaceutical products are based is a public good?

Exercise 1: Calculate the average price and standard deviation for each drug. What do you notice?

Table 2. Mean and standard deviation for each complete treatment for -19

	Remdesivir	Favipiravir	Lopinavir	Hidroxicloroquine	Cloroquine	Azithromicine	Sofosvubir	Pirfenidone	Tocilizumab
Mean	1.195,38	171,90	142,13	7,11	14,78	21,60	5.152,00	2.477,67	1.119,44
Standard deviation	949,78	68,92	140,72	6,40	25,35	19,36	5.420,58	2.602,49	947,38

Source: Own work

There are medicines with a very low average price (hydroxychloroquine, chloroquine and azithromycin), but there are also very expensive ones (remdesivir, pirfenidone, sofosvubir). Within a single drug, there is also wide variability between countries (perfenidone, tocilizumab).



Exercise 2: Calculate the mark-up ratio for each drug and each country, taking into account the price and cost data for the entire treatment. Also calculate the mean and standard deviation of the mark-up ratio for each drug:

$$\text{Mark-up ratio or Profit ratio} = \frac{\text{Price} - \text{Marginal cost}}{\text{Marginal cost}}$$

Table 4. Mark-up rate for complete Covid-19 treatment

	Remdesivir	Favipiravir	Lopinavir	Hidroxicloroquine	Cloroquine	Azithromicine	Sofosvubir	Pirfenidone	Tocilizumab
Bangladesh	65.67	-	-	2.00	-0.33	2.57	32.60	3.00	0.94
Brazil	65.67	-	-	-	-	12.57	856.80	-	-
China	65.67	10.55	3.25	18.00	15.67	4.00	-	43.48	4.49
Egypt	65.67	-	-	-	-	-	-	-	0.71
United States	345.67	-	124.75	17.00	309.00	44.00	3.721.00	308.87	8.53
France	259.00	-	23.25	4.00	-	30.43	-	74.61	-
India	65.67	4.64	9.00	1.00	2.33	2.57	0.40	2.23	1.27
Malasya	65.67	-	-	6.00	5.67	6.86	-	-	-
Pakistan	65.67	-	-	-	-	-	0.20	-	0.44
United Kingdom	259.00	-	35.00	3.00	25.67	6.86	1.565.40	81.61	1.57
South Africa	65.67	-	2.75	-	15.67	24.00	-	79.32	0.59
Sweden	259.00	-	42.00	2.00	12.33	10.43	-	69.84	-
Turkey	65.67	-	36.25	2.00	-	-	-	47.35	0.83
Mean	131.82	7.60	34.53	6.11	48.25	14.43	1.029.40	78.92	2.15
Standard deviation	105.53	3.10	34.92	6.15	84.34	13.62	1.083.86	83.73	2.43

Source: Own work

The lowest profit margin corresponds to tocilizumab, favipiravir, hydroxychloroquine and azithromycin. The highest profit margin corresponds to sofosvubir.

Exercise 3: Find the GDP per capita for each country (e.g. World Bank statistics) and compare the cost of the full treatment for VOC-19 with the GDP per capita of each country. Comment on the results.

Table 5. Percentage of complete treatment price with respect to per capita GDP.

	GDP (per capita \$)	Remdesivir	Favipiravir	Lopinavir	Hidroxicloroquine	Cloroquine	Azithromicine	Sofosvubir	Pirfenidone	Tocilizumab
Bangladesh	1.855,7	32,33	-	-	0,16	0,01	0,27	9,05	6,68	37,18
Brazil	8.717,2	6,88	-	-	-	-	0,22	49,20	-	-
China	10.261,7	5,85	2,25	0,17	0,19	0,05	0,07	-	13,44	19,00
Egypt	3.019,2	19,87	-	-	-	-	-	-	-	20,07
United States	65.297,5	4,78	-	0,77	0,03	0,14	0,10	28,50	14,71	5,18
France	40.493,9	5,78	-	0,24	0,01	-	0,11	-	5,79	-
India	2.099,6	28,58	5,37	1,91	0,10	0,05	0,24	0,33	4,76	38,39
Malasya	11.414,2	5,26	-	-	0,06	0,02	0,10	-	-	-
Pakistan	1.284,7	46,70	-	-	-	-	-	0,47	-	39,70
United Kingdom	42.330,1	5,53	-	0,34	0,01	0,02	0,03	18,50	6,05	2,16
South Africa	6.001,4	10,00	-	0,25	-	0,08	0,58	-	41,49	9,43
Sweden	51.615,0	4,53	-	0,33	0,01	0,01	0,03	-	4,25	-
Turkey	9.126,6	6,57	-	1,63	0,03	-	-	-	16,42	7,12

Source: Own work using data from [GDP per capita \(current US\\$\) | Data \(worldbank.org\)](https://data.worldbank.org/indicator/NY.GDP.PC.CD)

Treatment with some drugs is relatively expensive compared to the country's GDPpc: remdesivir accounts for 28% in India, 32% of GDPpc in Bangladesh, 46% in Pakistan; pirfenidone accounts for 16% in Turkey and 41% in South Africa.

Exercise 4: Reflect on the above results and suggest some measures that could improve affordability and access to treatment.



This analysis shows that medicines to treat Covid-19 could be manufactured at very low prices. If promising results from key clinical trials emerge, there is a possibility to increase production of generics and provide treatment to millions of people at very low unit prices. Other mechanisms are in place to optimise drug manufacturing. With joint procurement, a number of countries can order medicines together, to take advantage of economies of scale. There can be volume-price guarantees to purchase large quantities of medicines at fixed prices for a certain number of years.

Prequalification of major companies by the WHO can be recognized by any country as an indicator of the quality of the medicine, including adherence to good manufacturing practices and the stability or viability of the medicine over its stated shelf life, along with the bioequivalence of generic to branded versions.

There should be no intellectual property barriers preventing the mass production of these treatments worldwide. We need open 'technology transfer' so that the methods used to manufacture key medicines can be shared with any country that decides to produce them locally.

3. Conclusion and recommendations

This teaching experience has been very satisfactory, both from the point of view of the students' involvement and work, as well as their own assessment of the subject studied. In the first place, they have valued very positively the relevance of the project. Secondly, it has helped them to use international statistical portals that they had never used before. Thirdly, it has helped them to reflect on the difference between prices and costs, and how this difference translates into the profit margin.

Fourthly, they have carried out an in-depth reflection on the existing disparities in access to medicines. In this situation, they considered, by an overwhelming majority, that although patents aim to promote knowledge by creating a monopoly around the product or innovation developed, in the particular case of the Covid-19 pandemic, health should be prioritised, and therefore, there should be a free transfer of technology, not only at the level of medicines developed, but of all the trials carried out. It is essential that generic medicines are accessible to all people, because the health of some is good for the health of all (positive externality).

References

- [1] Li, G., De Clercq, E. (2020). Therapeutic options for the 2019 novel coronavirus (2019-nCoV). *Nature Reviews Drug Discovery*, 19 (3), 149-150.
- [2] Siegal, D., Hui, H., Doerffler, E., et al. (2017). Discovery and synthesis of a phosphoramidate prodrug of a pyrrolo[2,1-f][triazine-4-amino] adenine C-nucleoside (GS-5374) for the treatment of Ebola and emerging viruses. *Journal of Medicinal Chemistry* 60 (5), 1648-1661.
- [3] Hayden, F., Shindo, N. (2019). Influenza virus polymerase inhibitors in clinical development. *Current Opinion in Infectious Diseases*, 32 (2), 176-186.
- [4] Cao, B., Wang, Y., Wen, D. (2020). A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *New England Journal of Medicine*, 382, 1787-1799.
- [5] Yao, X., F. Ye, Zhang, M. (2020). In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clinical Infectious Diseases*, 71(15), 732-739.
- [6] IRCT (2020). A Prospective Randomized Controlled Clinical Trial Comparing the Therapeutic Efficacy of Sovodak (Sofosbuvir/Daclatasvir) with Standard Care in Patients with Moderate to Severe Coronavirus (COVID-19) Virus (2020). Registration Number: IRCT20200128046294N2.
- [7] WIPO (2017). An Improved Process for the Preparation of Pirfenidone. WO2017/122139. World Intellectual Property Office.
- [8] ClinicalTrials.gov (2020). Tocilizumab in COVID-19 Pneumonia (TOCOVID-19). NCT04317092. US National Library of Medicine.
- [9] Hill, A., Barber, M., Gotham, D. (2018). Estimated costs of production and potential prices for the WHO Essential Medicines List. *BMJ Global Health*, 3(1), e000571.
- [10] Hill, A., Wang, J., Levi, J., Heath, K., Fortunak, J. (2020). Minimum costs to manufacture new treatments for COVID-19. *Journal of Virus Eradication*, 6(2), 61-69.
- [11] Ortún, V. (2004). Patentes, regulación de precios e innovación en la industria farmacéutica. *Cuadernos Económicos de ICE*, 67, 191-2008.
- [12] Godwin, S., Varatharajan, D. (2006). Drug price differentials across different retail market settings. *Health Administrator*, 19, 41-47.