Estimated cost-based generic prices for investigational COVID-19 antivirals

Prepared by Melissa J Barber 1,2 and Dzintars Gotham 3

¹ Harvard T.H. Chan School of Public Health, Boston, USA, ² Harvard Graduate School of Arts and Sciences, Cambridge, USA, ³ King's College Hospital, NHS, United Kingdom

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1. Background

Information on the cost of production of medicines can help inform procurement negotiations. This brief provides estimates for production costs and estimated cost-based generic prices for investigational COVID-19 therapeutics.

The lack of transparency in medicine pricing has been a long-standing challenge for health systems. Without production cost or other comparative data, countries face asymmetric negotiations that compromise their ability to use health system resources effectively. The United States, through multilateral engagement, has supported calls to improve transparency across the pharmaceutical value chain: for example, World Health Assembly (WHA) resolution 72.8 on *Improving the transparency of markets for medicines, vaccines, and other health products* recognizes "that the types of information publicly available on data across the value chain of health products, including prices effectively paid by different actors and costs, vary among Member States and that the availability of comparable price information may facilitate efforts towards affordable and equitable access to health products." WHO pharmaceutical pricing policy guidelines strongly recommend that "countries use multiple pricing policies to achieve low prices for generic and biosimilar medicines that are informed by the cost of production."

2. Methods

The methods used here were developed in our earlier work. This work was originally commissioned by WHO for the Fair Pricing Forum in 2017,³ and has since been expanded and further developed to include medicines on the WHO Essential Medicines List,⁴⁻⁵ insulin including insulin analogues,⁶ HIV medicines and treatments

¹ WHO. WHA72.8 - Improving the transparency of markets for medicines, vaccines, and other health products. 2019. Available from: https://www.who.int/publications/m/item/wha72.8

² WHO. WHO guideline on country pharmaceutical pricing policies. 2020. Available from: https://apps.who.int/iris/rest/bitstreams/1309649/retrieve

³ WHO. At WHO Forum on Medicines, countries and civil society push for greater transparency and fairer prices. WHO. 2019; published online April 13. https://www.who.int/news/item/13-04-2019-at-who-forum-on-medicines-countries-and-civil-society-push-for-greater-transparency-and-fairer-prices

⁴ Hill A, Barber MJ, Gotham D. Estimated costs of production and potential prices for the WHO Essential Medicines List. *BMJ Global Health* 2018; 0: e000571.

⁵ Gotham D, Barber MJ, Hill AM. Estimation of cost-based prices for injectable medicines in the WHO Essential Medicines List. *BMJ Open* 2019: 9: e027780.

⁶ Gotham D, Barber MJ, Hill A. Production costs and potential prices for biosimilars of human insulin and insulin analogues. *BMJ Global Health* 2018; 3: e000850..

for opportunistic infections,⁷⁻⁸ direct-acting antivirals for hepatitis B^9 and hepatitis C,¹⁰⁻¹¹ antihypertensive medicines,¹² cancer medicines,¹³⁻¹⁶ and tuberculosis medicines.¹⁷⁻¹⁸

The costing algorithm includes costs of materials (active pharmaceutical ingredient, excipients), formulation costs, a 10% mark-up, and tax on profit.

The price of active pharmaceutical ingredient (API) is the most important determinant in the cost of a production of a medicine. In order to identify shipments of API, a proprietary export/import database (Panjiva) was searched for dates between Jan 2021 and March 2023, including import-export shipments from India, the United States, Mexico, Costa Rica, Panama, Bolivia, Brazil, Chile, Colombia, Ecuador, India, Paraguay, Peru, Uruguay, Venezuela, China, India, Indonesia, Pakistan, Sri Lanka, and the Philippines. ¹⁹ The search window ranged from 1 January 2019 to 1 March 2023. ²⁰

The search terms used were "baricitinib", "molnupiravir", and "nirmatrelvir OR Paxlovid OR bexovid", respectively.

Data on shipments were manually cleaned to exclude shipments that did not represent genuine API, using criteria developed in peer-reviewed publications (eg, shipments of working or reference standard, API with

⁷Barber M, Gotham D, Hill A. Cost-based estimated prices for key HIV, HCV, and MDR-TB medicines. Poster presentation at 23rd International AIDS Conference (AIDS 2020: Virtual), 6-10 July 2020.

⁸ Barber M, Gotham D, Hill A. Estimated cost-based generic prices for treatments of opportunistic infections. AIDS 2018, Amsterdam.

⁹ Hill A, Gotham D, Cooke G, Bhagani S, Andrieux-Meyer I, Cohn J, et al. Analysis of minimum target prices for production of entecavir to treat hepatitis B in high- and low-income countries. *J Virus Erad.* 2015;1(1):103–10.

¹⁰ Barber MJ, Gotham D, Khwairakpam G, Hill A. Price of a hepatitis C cure: Cost of production and current prices for direct-acting antivirals in 50 countries. *Journal of Virus Eradication* 2020; 6: 100001.

¹¹Hill A, Simmons B, Gotham D, Fortunak J. Significant reductions in costs of generic production of sofosbuvir and daclatasvir for hepatitis C. J Virus Eradication. 2016;1(2):28-31.

¹² MSF, Resolve to Save Lives. Under Pressure: Strategies to improve access to medicines to treat high blood pressure in low- and middle-income countries report. 2022 https://msfaccess.org/under-pressure-strategies-improve-access-antihypertensive-medicines-low-and-middle-income-0.

¹³ Hoen E, Meyer S, Durisch P, et al. Improving affordability of new essential cancer medicines. The Lancet Oncology 2019; 20: 1052–4.

¹⁴ Barber M, Gotham D, Hill A. Potential price reductions for cancer medicines on the WHO Essential Medicines List. 2017.

¹⁵ Hill A, Redd C, Gotham D, Erbacher I, Meldrum J, Harada R. Estimated generic prices of cancer medicines deemed cost-ineffective in England: a cost estimation analysis. *BMJ Open* 2017;(7):e011965.

¹⁶ Hill A, Gotham D, Fortunak J, et al. Target prices for mass production of tyrosine kinase inhibitors for global cancer treatment. BMJ Open. 2016(6):e009586.

¹⁷ Rockwood N, Cerrone M, Barber M, Hill AM, Pozniak AL. Global access of rifabutin for the treatment of tuberculosis—why should we prioritize this? *Journal of the International AIDS Society* 2019; 22: e25333.

¹⁸ Gotham D, Fortunak J, Pozniak A, Cooke G, Khoo S, Hill A. Estimated generic prices for novel treatments for drug-resistant tuberculosis. *J Antimicrob Chemother* 2017;72(4):1243–1252.

 $^{^{\}rm 19}$ Not all import data sources available for all dates.

 $^{^{20}}$ A reduced search window was used for ritonavir (Jan 1 2022 – Mar 1 2023) due to the volume of records. Ritonavir is an established generic drug with a large market.

impurities, finished product, etc).²¹ Outliers were defined as those with values higher than the third quartile plus 1.5 times the interquartile range, or lower than the first quartile minus 1.5 times the interquartile range, and were excluded. Weighted least-squares regression was used to fit linear models, with weights corresponding to shipment volume in kilograms. The outcome (unit cost) was log-transformed to reduce skew in the residuals. The predicted value on 1 December 2022 was used as the assumed average market price for API; we did not extrapolate beyond observed data.

Statistical analyses were performed and visualizations generated in R version 4.2.

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3. Results

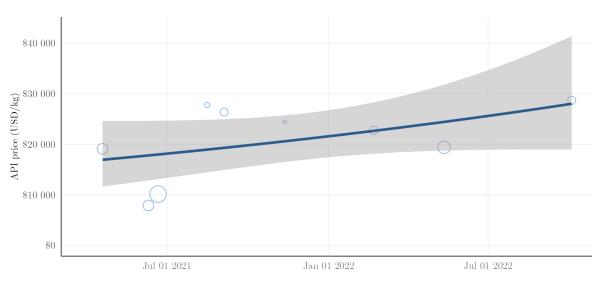
A. Baricitinib

After data cleaning, 9 shipments of baricitinib API were identified (Figure A1). The shipments represent a total 8.4 kg of API.

We used a generalized linear model GLM model to predict the price on 1 December 2022. These data suggest a current average API market price of US\$30,162/kg.

Assumed treatment regimen is 4mg baricitinib administered orally once daily for 14 days (14 doses total), sourced from WHO Therapeutics and COVID-19 living guidance.²²

Figure A1. Shipments of baricitinib API



shipment size (kg) \bigcirc 1 \bigcirc 2 \bigcirc 3

 $^{^{22}\} WHO\ The rapeutics\ and\ COVID-19\ living\ guidance.\ https://app.magicapp.org/\#/guideline/nBkO1E/rec/E5AOaN$

Figure A2. Estimated cost-based generic price for baricitinib

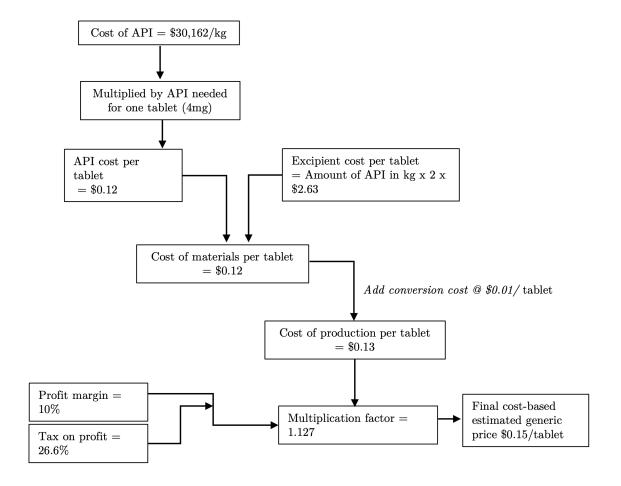


Table A1. Baricitinib cost of production and estimated cost-based generic prices (assuming current API market prices)

	4mg baricitinib	14 day treatment course:
	tablet	1x4mg baricitinib, 1x daily
Cost of production	\$0.13	\$1.83
Estimated cost-based generic price		
$(cost\ of\ production\ +\ 10\%\ profit\ margin$		
and 27% tax on profit)	\$0.15	\$2.06

Current costs and licensing status of baricitinib:

WHO issued a "strong recommendation" for baricitinib for patients with severe or critical COVID-19 on 14 January 2022.

The amount of API in the shipments captured is relatively small (8.4kg) in absolute terms. However, the dosage of baricitinib is low (4mg), and therefore the total volume of shipments nevertheless represents a significant quantity of API for this drug (enough to manufacture 2.1 million 4 mg pills or 150,000 treatment courses for COVID-19).

Eli Lilly's list price of \$1,109.92 per 14 day treatment course of baricitinib 4mg is 539x the cost-based estimated generic price (\$2.06).²³ Baricitinib is already approved for rheumatoid arthritis. Global prices range widely.

Table A2. Baricitinib 4mg tablet prices, by country

			Price per	Price per
		Price	tablet	treatment course
Country	Generic?	(local currency)	$(\$\mathrm{USD})$	(\$USD)
India^{24}	Yes - Natco	INR 30 per tab	\$0.41	\$5.74
${ m Bangladesh^{25}}$	Yes- Beximco	BDT 40.00 per tab	\$0.47	\$6.58
France^{26}	No – Eli Lilly	EUR 651.15 (28 tabs)	\$26.57	\$371.98
United				
$ m Kingdom^{27}$	No – Eli Lilly	GBP 805.56 (28 tabs)	\$39.38	\$551.32
$\mathrm{Denmark}^{28}$	No – Eli Lilly	DKK 8818.35 (28 tabs)	\$48.36	\$677.04
		Not available in 4mg.		
United States		Assuming 2x2mg. USD		
$(\mathrm{VA})^{29}$	No – Eli Lilly	1,763.04 (30 2 mg tabs)	\$58.77	\$822.78
${ m Argentina^{30}}$	No – Eli Lilly	ARS 184,100.84 (28 tabs)	\$63.32	\$886.48
US list price	No – Eli Lilly	USD $2,378.40 (30 \text{ tabs})$	\$79.28	\$1,109.92

²³ This assumes bottles can be split across patients; Eli Lilly's product usually is packaged in bottles of 30 or 28 tablets.

 $^{^{24}\} https://medical$ dialogues.in/news/industry/pharma/natco-pharma-launches-baricitinib-in-india-without-patent-waiver-approval-77354

²⁵ https://medex.com.bd/brands/31905/barri-4mg

 $^{^{26}}$ https://base-donnees-publique.medicaments.gouv.fr/extrait.php?specid=61751780

 $^{^{\}rm 27}~{\rm https://bnf.nice.org.uk/medicinal-forms/baricitinib.html}$

 $^{^{28}\ \}mathrm{https://www.medicinpriser.dk/Default.aspx}$

 $^{^{29}\ \}mathrm{https://www.vendorportal.ecms.va.gov/nac/Pharma/List}$

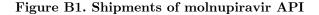
 $^{^{30}\ \}mathrm{https://servicios.pami.org.ar/vademecum/views/consultaPublica/listado.zul}$

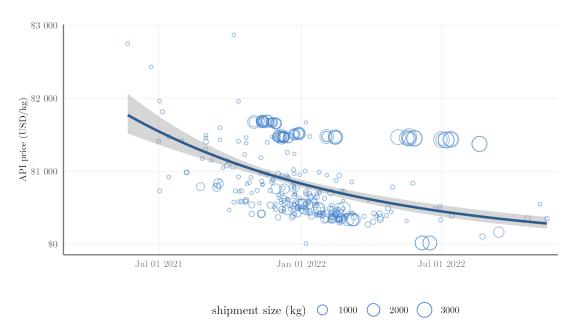
B. Molnupiravir

After data cleaning, 324 shipments of molnupiravir API were identified. The shipments represent a total 164,000 kg of API.

We used a generalized linear model GLM model to predict the price on 1 December 2022. These data suggest a current average API market price of US\$900/kg.

Assumed treatment regimen is 800mg molnupiravir administered orally every 12 hours for 5 days (10 doses total), sourced from the Phase 3 MOVe-OUT trial quoted in the press release.³¹





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 $^{^{31}~\}mathrm{https://clinicaltrials.gov/ct2/show/NCT04575597}$

Figure B2. Estimated cost-based generic price for molnupiravir

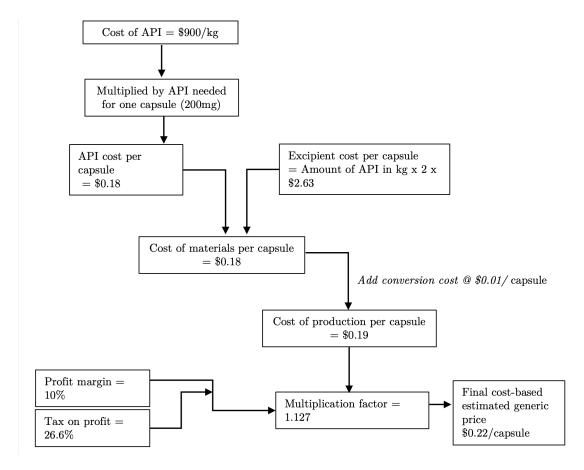


Table B1. Molnupiravir cost of production and estimated cost-based generic prices, assuming current API market prices

	$200 \mathrm{mg}$	5 day treatment course
	molnupiravir	4x200mg molnupiravir, $2x$
	capsule	daily
Cost of production	\$0.19	\$0.22
Estimated cost-based generic price		
$(cost\ of\ production\ +\ 10\%\ profit\ margin$		
and 27% tax on profit)	\$7.64	\$8.61

A note on costs and process optimization:

An April 2021 analysis of the industrial synthesis of molnupiravir, by Ahlqvist et al at the Massachusetts Institute of Technology (MIT), independently estimated the cost of production for the active ingredient.

Ahlqvist et al estimated that, starting from raw materials and using an optimized synthetic process, molnupiravir active ingredient would cost US\$427-799/kg to manufacture.³²

Table B2. Cost of production and estimated cost-based generic prices, assuming Ahlqvist et al estimated for optimized production:

	Optimization assumption	200mg molnupiravir capsule	5 day treatment course: 4x200mg molnupiravir, 2x daily
	With 75% solvent	ФО 10	Ф 2 9 <i>C</i>
Cost of production	recycling Without 75%	\$0.10	\$3.86
	solvent recycling	\$0.17	\$6.84
	With 75% solvent		
Estimated cost-based generic price	recycling	\$0.11	\$4.35
$(cost\ of\ production\ +\ 10\%\ profit$	Without 75%		
margin and 27% tax on profit)	solvent recycling	\$0.19	\$7.70

Current costs and licensing status of molnupiravir:

The US FDA narrowly approved an emergency use authorization (EUA) for molnupiravir, authorizing use for "the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct SARS-CoV-2 viral testing who are at high risk for progressing to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate."³³

Merck announced on 27 April 2021 that they had entered into non-exclusive voluntary licensing agreements for molnupiravir with five Indian generics manufacturers (Cipla Limited, Dr. Reddy's Laboratories Limited, Emcure Pharmaceuticals Limited, Hetero Labs Limited and Sun Pharmaceutical Industries Limited).

The US government has ordered 1.7 million treatment courses, at about \$700/patient.³⁴ The UK has ordered 480,000 courses, at unknown cost.³⁵ France ordered 50,000 but has since cancelled the order, citing concerns about efficacy.³⁶

The US price per course (\$700) is 81x the estimated cost per regimen (\$8.61).

³² See page 3 of supplementary information, Ahlqvist et al. "Progress Towards a Large-Scale Synthesis of Molnupiravir (MK-4482, EIDD 2801) from Cytidine". https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8153789/

 $^{^{31}\} https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization$

 $^{^{32}\} https://www.nytimes.com/live/2021/09/30/world/covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines\#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merck-antiviral-pill-covid-delta-variant-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-vaccines#merch-antiviral-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-delta-pill-covid-$

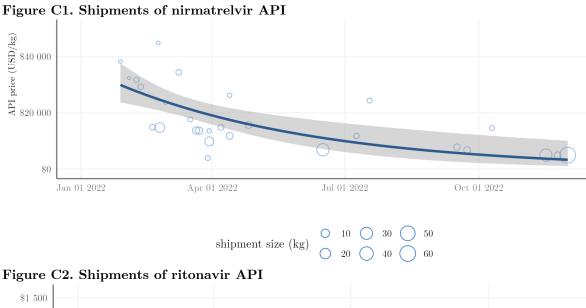
 $^{^{\}rm 33}$ https://www.bbc.co.uk/news/health-59163899

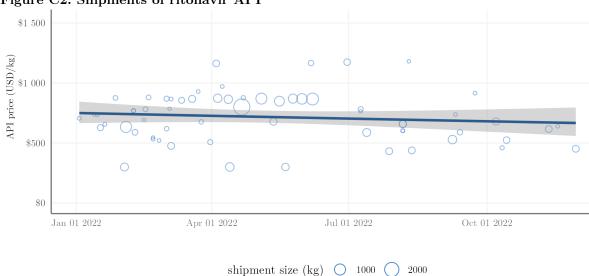
 $^{^{34}}$ https://www.has-sante.fr/jcms/p_3304161/fr/covid-19-deux-nouveaux-traitements-evalues-par-la-has

C. Nirmatrelvir/ritonavir

After data cleaning, 30 shipments of nirmatrelvir and 63 shipments of ritonavir API were identified, amounting to 228 kg of nirmatrelvir API and 14,394 kg of ritonavir API. We used a generalized linear model GLM model to predict the price on 1 December 2022. These data suggest a current average API market price of US\$4944/kg for nirmatrelvir and US\$657/kg for ritonavir.

Assumed treatment regimen is 2x150mg nirmatrelvir + 1x100mg ritonavir administered orally twice daily for 5 days, sourced from the FDA Emergency Use Authorization.³⁷





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 $^{^{35}\ \}mathrm{https://www.fda.gov/media/155050/download}$

Figure C3. Estimated cost-based generic price for nirmatrelvir

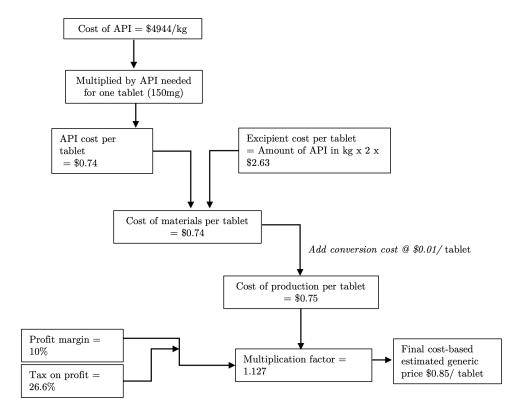


Figure C4. Estimated cost-based generic price for ritonavir

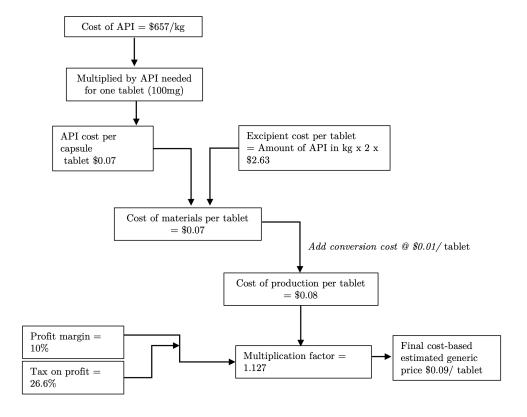


Table C1. Nirmatrelvir/ritonavir cost of production and estimated cost-based generic prices (assuming current API market prices)

			5 day treatment course: 2x150mg nirmatrelvir +
	drug	tablet	1x100mg ritonavir 2x daily
Cost of any dustion	nirmatrelvir 150mg	\$0.75	
Cost of production	ritonavir 100mg	\$0.08	\$15.81
Estimated cost-based generic price	nirmatrelvir 150mg	\$0.85	
$(cost\ of\ production\ +\ 10\%\ profit$	ritonavir 100mg	\$0.09	\$17.82
margin and 27% tax on profit)			

Current costs and licensing status of nirmatrelvir/ritonavir:

WHO has recommended nirmatrelvir/ritonavir for mild and moderate COVID-19 patients at highest risk of hospital admission.³⁶ The FDA has issued emergency use authorization and the EMA has issued conditional marketing authorization.³⁸ Transparency in the cost of production may be helpful as health systems seek to purchase the medicine.

Phase 2/3 of EPIC-HR (n=2246, non-hospitalized adults at high risk) showed a 89% reduction in hospitalization or death when taken within 3 days of onset (88% if taken within 5 days of system onset) compared to placebo.³⁹ There is not yet evidence on its effectiveness in other populations; the release of results from PANORAMIC will guide future use.

Significant supply constraints remain. KEI has created a helpful database tracking publicly announced purchases of Paxlovid.⁴⁰ According to their analysis, 98.2% of Pfizer's projected supply capacity for 2022 was accounted for by orders from only 18 countries (mostly high-income countries), suggesting that without significant expansion of supply by Pfizer or generic manufacturers, access for other countries remains very limited. This prediction has sadly proven to be true.

The amount of nirmatrelvir API in the shipments captured is relatively small (~228kg), equivalent to 1.5 million pills or 76,000 treatment courses. This analysis should be interpreted both with caution, and as a conservative estimate (i.e. erring on the side of estimating higher, rather than lower). Given 1) trends observed with other patented products as they shift to generic production and 2)

 $^{^{36}}$ https://www.ema.europa.eu/en/news/ema-receives-application-conditional-marketing-authorisation-paxlovid-pf-07321332-ritonavir-treating

³⁷ https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-additional-phase-23-study-results

 $^{^{39}}$ https://www.nejm.org/doi/full/10.1056/NEJMoa2118542

 $^{^{40}}$ KEI. Paxlovid procurement announcements. $https://docs.google.com/spreadsheets/d/1fE1sB6VwrrqGTXReJb29IH_b-B6yeOhFRzsg0_D1GrQ/edit?usp=sharing$

anticipated process optimization over time, we expect global API costs and therefore cost of production to decrease if numerous nirmatrelvir generics become available.

Table C2. Nirmatrelvir/ritonavir prices, by country – Source: KEI⁴¹

			Price per 5 day treatment
Country	Courses	Date announced	course (\$US)
Australia ⁴²	500,000	17 Oct 2021	<u>, , , , , , , , , , , , , , , , , , , </u>
United Kingdom ⁴³	250,000	20 Oct 2021	
United States ⁴⁴	10,000,000	18 Nov 2021	\$530
Canada^{45}	1,000,000	3 Dec 2021	
New Zealand 46	60,000	$5~{\rm Dec}~2021$	
$ m Japan^{47}$	2,000,000	$17~{\rm Dec}~2021$	
United Kingdom ⁴⁸	2,500,000	$22~{\rm Dec}~2021$	\$502.5
France^{49}	500,000	$22~{\rm Dec}~2021$	
Israel^{50}	100,000	$25~{\rm Dec}~2021$	
South $Korea^{51}$	362,000	$27~{\rm Dec}~2021$	
$\mathrm{Germany}^{52}$	1,000,000	$28 \mathrm{Dec} 2021$	
$\mathrm{Belgium}^{53}$	10,000	3 Jan 2022	
United States 54	10,000,000	4 Jan 2022	\$530
South Korea 55	400,000	5 Jan 2022	
$ m Mexico^{56}$	n/a	7 Jan 2022	
Czech Republic 57	50,000	8 Jan 2022	
$ m Italy^{58}$	200,000	$9~{\rm Jan}~2022$	

 $^{^{41}}$ KEI. Paxlovid procurement announcements. $https://docs.google.com/spreadsheets/d/1fE1sB6VwrrqGTXReJb29IH_b-B6yeOhFRzsg0_D1GrQ/edit?usp=sharing$

 $^{^{42}\} https://www.health.gov.au/ministers/the-hon-greg-hunt-mp/media/australia-secures-additional-covid-19-treatments$

⁴³ https://www.reuters.com/world/uk/britain-secures-covid-19-antivirals-merck-pfizer-2021-10-20/

 $^{^{44}\} https://www.hhs.gov/about/news/2021/11/18/biden-administration-secures-10-million-courses-pfizers-covid-19-oral-antiviral-medicine-as-additional-tool-reduce-hospitalizations-save-lives.html$

 $^{^{45}\} https://www.canada.ca/en/public-services-procurement/news/2021/12/government-of-canada-signs-agreements-for-covid-19-oral-antiviral-treatments.html$

 $^{^{46} \} https://www.youtube.com/watch?v=cpvkV5tlfUk\&ab_channel=MinistryofHealth-Manat\%C5\%ABHauoranderschaften (Compared to the compared to t$

⁴⁷ https://www.voanews.com/a/japan-seeks-additional-vaccines-for-covid-19-booster-campaign-/6359260.html

⁴⁸ https://www.pfizer.com/news/press-release/press-release-detail/pfizer-provide-united-kingdom-additional-25-million

⁴⁹ https://www.connexionfrance.com/French-news/New-anti-Covid-pill-approved-in-France-first-delivery-due-next-week

 $^{^{50}\} https://www.reuters.com/world/middle-east/israel-orders-pfizers-new-covid-19-pill-2021-12-25/2021-12-$

 $^{^{51}~\}rm{https://en.yna.co.kr/view/AEN20211227004551320}$

⁵² https://www.dw.com/en/germany-buys-1-million-doses-of-anti-covid-pill-paxlovid/a-60276666

⁵³ https://www.vrt.be/vrtnws/en/2022/01/03/belgium-buys-10-000-courses-of-pfizer-coronavirus-drug/

 $^{^{54}\} https://www.pfizer.com/news/press-release/press-release-detail/pfizer-provide-us-government-additional-10-million$

 $^{^{55}\ \}text{https://www.reuters.com/world/asia-pacific/south-korea-agrees-buy-additional-pfizer-covid-19-pills-2022-01-05/properties agrees-buy-additional-pfizer-covid-19-pills-2022-01-05/properties agrees-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-2022-01-05/properties-buy-additional-pfizer-covid-19-pills-202-01-05/properties-buy-additional-pfizer-covid-19-pills-202-01-05/properties-buy-additional-pfizer-covid-19-pills-202-01-05/properties-buy-additional-pfizer-covid-19-pills-202-01-05/properties-buy-additional-pfizer-covid-19-pills-202-01-05/properties-buy-additional-pfizer-covid-19-pills-202-01-05/properties-buy-additional-pfizer-buy-additional-pfizer-buy-additional-pfizer-buy-additional-pfizer-buy-additional-pfizer-buy-additional-pfizer-buy-additional-pfizer-buy-additional-p$

 $^{^{56}} https://www.youtube.com/watch?v=14EDsSsmSPI\&t=2499s\&ab_channel=Andr\%C3\%A9sManuelL\%C3\%B3pezObrador\&themeRefresh=1$

⁵⁷ https://english.radio.cz/czechia-buy-50000-packs-pfizers-paxlovid-covid-19-medication-8738676

 $^{^{58}\} https://www.reuters.com/business/healthcare-pharmaceuticals/italy-receive-40000-merck-antiviral-drug-doses-next-week-official-2022-01-09/$

${ m Spain}^{59}$	344,000	$10 \ \mathrm{Jan} \ 2022$	
$Taiwan^{60}$	20,000	$15~\mathrm{Jan}~2022$	
Panama^{61}	54,000	$25~\mathrm{Jan}~2022$	\$250
${ m Malaysia^{62}}$	110,000	$4~{\rm Mar}~2022$	
$Taiwan^{63}$	350,000	11 Apr 2022	

 $^{^{59}\} https://www.elespanol.com/ciencia/salud/20220110/paxlovid-pastilla-revolucionaria-pfizer-contra-covid-llega-espana/641435924_0.html~and~https://www.sanidad.gob.es/gabinete/notasPrensa.do?id=5624$

⁶⁰ https://focustaiwan.tw/society/202201150009

 $^{^{61}\} https://www.laestrella.com.pa/nacional/220125/consejo-gabinete-aprueba-compra-antiviral-paxlovid-pfizer$

 $^{^{62}\} https://www.thestar.com.my/news/nation/2022/03/05/covid-19-watch-110000-high-risk-patients-to-get-first-batch-of-oral-antiviral-paxlovid-says-khairy$

⁶³ https://focustaiwan.tw/society/202204110017

D. Remdesivir

After data cleaning, 57 shipments of remdesivir API were identified. The shipments represent a total 406 kg of API.

We used a generalized linear model GLM model to predict the price on 1 December 2022. These data suggest a current average API market price of US\$6080/kg.

Assumed treatment regimen is one dose daily for 10 consecutive days, including 200 mg remdesivir administered intravenously on day 1, followed by 100mg intravenously for 3, 5, or 10 days (depending on the patient and varying across national guidelines). WHO has issued a conditional recommendation that remdesivir demonstrates a modest benefit in patients with severe, but not critical COVID-19.64

 $^{64}\ WHO\ The rapeutics\ and\ COVID-19\ living\ guidance.\ \underline{https://app.magicapp.org/\#/guideline/nBkO1E/rec/E5AOaN}$

Figure D1. Shipments of remdesivir API

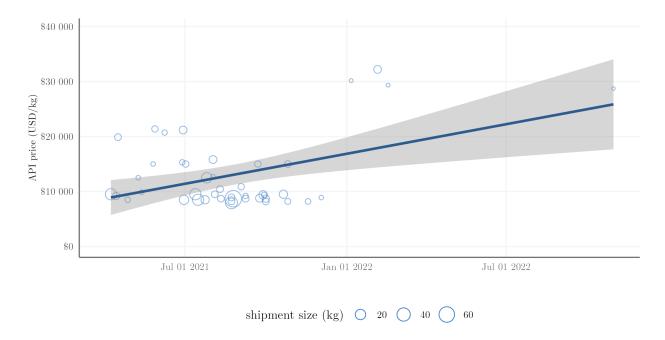


Figure D2. Estimated cost-based generic price for remdesivir

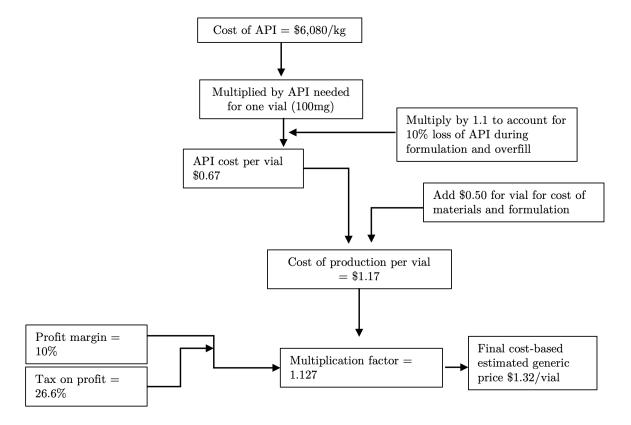


Table D1. Remdesivir cost of production and estimated cost-based generic prices, assuming current API market prices

	100mg	2x100mg remdesivir day 1, 1 x 100mg following da		
	remdesivir vial	$3 \ days$	5 days	10 days
Cost of production Estimated cost-based generic price (cost of production + 10% profit	\$1.17	\$4.68	\$7.01	\$12.86
margin and 27% tax on profit)	\$1.32	\$5.27	\$7.90	\$14.49

Current costs and licensing status of remdesivir:

The United States Food & Drug Administration approved remdesivir for use in adults and pediatric patients 12 years of age and older requiring hospitalization in October 2022. In January 2020, this indication was expanded to use in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

Gilead has not licensed remdesivir to the MPP. Limited bilateral licenses have been signed; the licenses have not been made public for public scrutiny 65

The US price per course (\$2,340) is 296x the estimated cost-based estimated generic price per 5 day regimen (\$7.90).

 $[\]frac{65}{\rm https://www.gilead.com/news-and-press/press-room/press-releases/2021/4/gilead-sciences-announces-steps-to-expand-availability-of-remdesivir-in-india}$

⁶⁶ https://www.bbc.co.uk/news/world-us-canada-53254487