

Access Challenges to COVID-19 Therapeutic Candidates
Briefing Document
Edition #1: last updated 2020 May 27

Contents

INTRODUCTION	1
OVERCOMING EXCLUSIVITY BARRIERS TO COVID-19 THERAPEUTICS	1
Patents	2
Data and Market Exclusivity.....	2
Policy and Legal Safeguards	2
DRUGS/TREATMENTS:	3
Remdesivir	3
Tocilizumab	6
Lopinavir/ritonavir (LPV/r)	7
Favipiravir.....	8
SUMMARY TABLE	9

INTRODUCTION

The current global pandemic of COVID-19, caused by infection with the novel coronavirus SARS-CoV-2, poses an unprecedented global health challenge. There are no proven effective treatments or vaccines to date. More than 70 [therapeutic candidates](#) are in different stages of clinical trials. The World Health Organization (WHO) launched the international [Solidarity Trial](#) on selected therapeutic candidates. Once safety and efficacy of any of the candidate therapeutics are demonstrated, ensuring access to the effective therapeutics for all people will be an immediate challenge facing all countries. To ensure universal access to effective COVID-19 medicines in a timely manner, massive production and sufficient supply of quality-assured medicines, and equitable allocation based on public health needs, will be required at both international and national levels.

This briefing document aims to provide an up-to-date analysis of the main access challenges associated with selected priority therapeutic candidates for COVID-19 treatment. For each candidate, key information including medical attributes, patents and other exclusivity rights, supply situation, and pricing are provided. A colour-coded summary table indicates levels of supply constraints. All information is collected from publicly available sources and analysed independently by MSF Access Campaign. The choice of the selected priority candidates and the related information will be updated regularly; **please refer to last updated date at top of document.**

This briefing document offers only a shortlist of candidate therapeutics; a number of other medicines are also under evaluation in numerous clinical trials around the world.

OVERCOMING EXCLUSIVITY BARRIERS TO COVID-19 THERAPEUTICS

Multiple barriers may hinder rapid and ample production and sufficient supply of effective and affordable therapeutics. At the centre is the use of intellectual property (IP) and other exclusivities to restrict manufacturing and supply options, delaying competition that would lower drug prices and increase patient access. Market dominance including monopolies held by pharmaceutical corporations through patents and other types of IP and regulatory exclusivities may prevent other manufacturers from increasing global manufacturing capacity. These exclusivities may also enable companies to

charge high prices and profiteer from the pandemic or prioritise wealthier countries over ones with less financial capacity. Also, the absence of platforms for open sharing and the right to use of know-how, data and IP can impact technology transfer and access to critical technologies, and may further delay the development and eventual regulatory approval of affordable generic or biosimilar products.

Patents

Patents are territorial rights granted by national government agencies allowing for a maximum 20-year monopoly for the patent holder. However, in some countries, this monopoly could be further extended beyond 20 years through patent terms extensions and other exclusivities. Once granted, patent can exclude anyone from using, producing and selling the concerned product without the permission of the patent holder. Companies often apply for multiple patents on the same medicine to prolong the market monopoly – known as “patent evergreening”. Patents could also be applied for by companies on second medical indications of a repurposed medicine. Companies could engage in bilateral secret voluntary licenses of its IP and technology to specific manufacturers while excluding others despite the potential need to ramp up global production. Transparency and accountability are lacking with respect to their actions or license agreements, in particular whether they are aligned with global public health needs and inclusion of all countries or not.

Data and Market Exclusivity

In addition to patents, companies may also apply for or may receive exclusive rights during the regulatory process, including but not limited to data exclusivity and market exclusivity associated with orphan drug status of the medicine. [Data exclusivity](#) prohibits regulatory agencies (within a fixed period of time, and when reviewing registration dossiers submitted by generic or biosimilar producers) from registering even if they do not directly rely on the test data submitted by the originator company. In some countries, regulators will refuse to review dossiers of generic-drug companies without data from the originator company being submitted first, which some companies are reluctant to do in low- and middle-income countries. Moreover, some countries allow for data exclusivity for a new medical indication for an old repurposed medicine. Market exclusivity associated with orphan drug status and other designations prevent any alternative producers from supplying the concerned medicine for a certain period of time. Both data exclusivity and market exclusivity provide additional monopoly power alongside patents and may delay product competition and availability of affordable generic formulations of a medicine, even after the 20-year term of the patent is over.

Policy and Legal Safeguards

To overcome barriers of market dominance and access to patented health technologies and products needed for COVID-19 treatments, countries can make use of a range of public health safeguards enshrined in international law. In particular, flexibilities are contained in the Agreements on Trade-related Intellectual Property Rights (TRIPS) and the Doha Declaration on TRIPS and Public Health. [Important measures](#) that can be adapted at national, regional and international levels include but are not limited to:

- Issuing [compulsory licenses and government-use licenses](#) to allow local production, importation and exportation of patented medical tools within a defined period of time, including exploring a regional approach to compulsory licensing to facilitate international collaboration and adapting expedited procedures to allow fast-track compulsory licenses
- Adapting strict patentability criteria, under national or regional arrangements, to prevent patenting on new indications, methods of use and derivatives of medicines
- Suspending the application of data exclusivity and other market exclusivities (or providing waivers), if existing in national or regional laws, to enable rapid regulatory approval of generic and biosimilar products
- Suspending certain obligations under bilateral or regional trade and investment agreements that may constrain a country’s ability to issue a compulsory license, undermine strict patent examination criteria, and facilitate data or other exclusivities on medicines

The global impact of the COVID-19 pandemic also presents challenges and limitations of relying only on national strategies to ensure an effective global response. In this regard, countries should explore effective international collaborations and binding agreements under the United Nations to facilitate open sharing of technologies, know-how, data, and global non-exclusive rights to use and produce COVID-19 medicines.

For more information of MSF positions and recommendations in this regard, please visit: <https://msfaccess.org/covid-19-action>

DRUGS/TREATMENTS:

Remdesivir

Overview

Remdesivir, first manufactured by pharmaceutical corporation Gilead Sciences, is one of the antiviral drugs currently in clinical trials for the treatment of COVID-19 and is the only new experimental COVID-19 drug. It has not been approved for any other indication anywhere in the world. Gilead holds primary patents on the drug in more than 70 countries that may block generic entry until 2031.

Gilead has a poor track record for facilitating affordable and sustained access to lifesaving treatments. MSF has seen firsthand what Gilead's greed does to people with HIV and hepatitis C all over the world as the company's prices and intellectual property strategies keep lifesaving medicines out of reach, particularly in middle-income countries who have been systematically excluded from the scope of its voluntary licenses. The company's recent actions with remdesivir provide scant assurance that the company can be trusted to act in the public interest.

Any potential COVID-19 treatment must be available, accessible and affordable for everyone once they are developed. While awaiting results of the trials with remdesivir, Gilead should announce now that it will not enforce its patents that it has applied for and obtained over the last few years. When prevented or restricted by patents and other exclusivity rights enforced by Gilead, generic production could be prevented for years. Early entry of generic production is vital to secure alternative suppliers and increase global production capacity of the drug available to supply all countries around the world. Although Gilead recently shared information about its current production capacity, the corporation has not clarified its relationships with generic manufacturers, and there are concerns that Gilead's decision to keep full control over remdesivir via exclusive intellectual property and secret commercial agreements with generic producers will lead to insufficient manufacturing capacity to supply for global needs as well as unaffordable prices for resource-limited countries.

Medical and Clinical Trials

Remdesivir, an antiviral drug that requires cold chain and must be given via intravenous route, was originally developed to treat Ebola virus but without positive results. In vitro studies against SARS-CoV-2, the virus that causes COVID-19, show potent antiviral action. Several publications on remdesivir have been released recently. First, a case series of 53 selected patients hospitalised with severe COVID-19 who received remdesivir under compassionate use was published, but no conclusions can be drawn. Next, the results of the first randomised clinical trial were published. This was a multicentric, placebo-controlled trial of severe cases in China. Although the study was well conducted, little more than half of the targeted sample size was achieved (237 out of 453). Since the study was underpowered due to limited sample size, and the number of people required for a clinical trial is determined based on statistical calculations, no conclusion can be drawn from this data.

More recently, a press release from the US National Institutes of Health (NIH) reported preliminary results from another randomised clinical trial of 1,063 hospitalised patients. The results showed statistical evidence for a shorter time to recovery among those who received remdesivir (from 15 to 11 days), but there is no clear survival benefit. Statistical evidence, however, may suggest a potential survival benefit. While the drug still may be promising in certain populations, particularly if started earlier in the course of disease, at this point it cannot be considered a game changer. The full data and analysis from the NIH trial are needed to allow for proper judgment, which surprisingly still has not yet been made public at the time of writing. Nonetheless, the drug received [approval for emergency use from the United States Food and Drug Administration \(US FDA\)](#) on 1 May 2020 based on this trial, with the requirement that the US government control distribution and allocation within the US. [The European Medicines Agency \(EMA\) has also started a rolling review of remdesivir](#), which will include a benefit-risk analysis. On 7 May 2020 the [Japanese regulatory agency](#) granted exceptional approval for remdesivir to be used for the treatment of severe COVID-19. On 26 May 2020, remdesivir was approved by the [UK regulatory agency](#) for limited use in patients meeting certain criteria.

Remdesivir is being tested as part of the ongoing World Health Organization (WHO)-sponsored multi-country randomised clinical trial ('SOLIDARITY') that launched in March 2020, as well as in other clinical trials in China, US and Europe.

Patents

The primary patent on the base compound of remdesivir has been granted to Gilead in more than 70 countries, which, if enforced, will block the entry of generic producers until 2031. These patents set Gilead up to control the production and supply, and charge whatever they want during this global health crisis and for years to come. [Gilead has also applied for secondary patents covering the use of remdesivir for the treatment of other coronaviruses \(SARS, MERS\) in many countries.](#)

Despite the announcement of public health emergency declarations across the US since the end of February 2020, Gilead still sought an orphan drug designation from the US FDA on remdesivir that would have allowed for even longer monopoly control over the 20-year patents it had already filed. Gilead only gave up this special designation in late March [following intense criticism from civil society groups and MSF](#). Gilead has yet to commit to not enforcing its patents globally despite [an open request by more than 150 civil society organisations, including MSF, and individuals around the world](#).

If remdesivir is found to be effective and is approved, Gilead should not be allowed to enforce its patents nor claim any other types of exclusivities over remdesivir. No company should profiteer off this pandemic.

Several generic companies in China (BrightGene, CobenPharm, Hainan Haiyao, Sichuan Kelun, Hunan Warran), one Taiwanese research institute (National Health Institute) and one generic company in Bangladesh (Beximco) have announced that they already have the capacity to produce remdesivir, and some have proceeded to test their production of the active pharmaceutical ingredients and finished product.

However, Gilead has secretly negotiated and signed voluntary licenses with generic companies from India and Pakistan, as the corporation has done in the past with HIV and hepatitis C medicines. On 12 May 2020, Gilead [announced](#) that it had entered into agreements with five generic manufacturers in India and Pakistan who can market generic versions of the drug in 116 countries and 11 territories, not 127 countries as announced by the company. The licenses, however, exclude nearly half of the world's [population](#), including most South American countries and a number of middle-income countries that have considerable manufacturing capacity, such as Brazil and Russia, where coronavirus cases are surging, and China, where the first coronavirus epicenter was located and a country that supported the first phase-III clinical trials of remdesivir.¹ Negotiated in the dark, there is no transparency around the terms and conditions of the agreements, including whether or not they are aligned with public health needs.

MSF has witnessed first-hand the impact that Gilead's corporate policies have had on people with hepatitis C. Gilead notoriously set the price for a hepatitis C treatment at an exorbitant US\$1,000 per pill in 2013 in the US. Gilead then negotiated bilateral voluntary licenses with Indian manufacturing companies that excluded high- and middle-income countries like Brazil and China from receiving generic supply, leaving these countries to negotiate directly with the company, largely in secret, and having to pay higher prices.

This "business as usual" approach by pharmaceutical corporations is unacceptable: there should be no enforcement of patents during a pandemic, and we cannot rely on pharmaceutical companies' willingness, even in exchange for massive public funding, to address public health needs and to deliver an effective global response to the COVID-19 pandemic. Any agreements should be made public and licenses must include a worldwide right to use by all countries – low-, middle- and high-income countries alike. More importantly, the precedent set by Gilead should alert Member States and WHO that we cannot rely on the voluntary actions of companies in this pandemic and we must [adopt binding measures](#) to ensure global access to COVID19 medical tools.

¹ Countries and regions excluded from the license include: Albania, American Samoa, Argentina, Bolivia, Bosnia-Herzegovina, Brazil, Bulgaria, Chile, China, Colombia, Congo, Ecuador, Gaza and the West Bank, Iran, Iraq, Jordan, Kosovo, Lebanon, Macedonia, Malaysia, Mexico, Montenegro, Paraguay, Peru, Romania, Russia, Serbia, Syria, Turkey, Uruguay, Venezuela, and Yemen.

In addition, if required in the interest of public health, countries must make use of legal tools like ‘compulsory licenses’ to override patents during this pandemic and access the drug in the quantities needed. Already, Brazil, Canada, Chile, Ecuador and Germany have taken steps to facilitate issuing of compulsory licenses for COVID-19 medicines, vaccines and other medical tools. Similarly, Israel issued a compulsory license for patents on another medicine they were investigating for COVID-19.

Pricing

The price of remdesivir is unknown. However, as the drug entered clinical trials in China for COVID-19 in February 2020, it was estimated that [Gilead may charge US\\$260 per treatment course in the country](#). The price has been estimated to be US\$900-\$1,000 per treatment course in the US, although it may well be higher. In the US, the Institute for Clinical and Economic Review (ICER) [indicated](#) that it would be considered cost effective at US\$4,460 per treatment if it shows a benefit in mortality, but only US\$390 if it only shortens the hospital stay. A recent pricing study, however, estimated the manufacturing cost of remdesivir to be less than [US\\$9](#) for a full treatment course, suggesting that this potential COVID-19 treatment could be made available to all at an affordable price during this pandemic.

Public Funding and Contributions

The R&D of remdesivir is the result of a massive collective effort, involving many actors and multiple public resources. Remdesivir was developed with considerable public funding, mainly from the US government. [Millions of taxpayer dollars have been invested by different US public agencies](#) including the US Department of Defense, Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), and National Institute of Allergy and Infectious Diseases (NIAID) towards the development of remdesivir. US-based non-profit organisation Public Citizen [estimates](#) that taxpayers have contributed more than US\$70.5 million to the development of remdesivir so far.

Public health authorities and regulatory bodies in many other countries have also supported the ongoing clinical trials. People with COVID-19 and healthcare workers are indispensable contributors, as the clinical trials would not be possible without them. It is unacceptable for remdesivir to be put under one company’s exclusive control, especially considering that the drug was developed with considerable public funding for both early-stage research and clinical trials, and due to the extraordinary efforts and personal risks healthcare workers and patients have faced using the medicine in clinical trial settings. If its efficacy is demonstrated, patents on remdesivir should be overridden so that the drug can be affordable to everyone.

Supply

Following [pressure from civil society](#) (including MSF) demanding Gilead disclose its manufacturing capacity and existing supply of remdesivir, Gilead [announced](#) on 4 April that they will have 1.5 million individual doses of the drug by the end of May 2020 – enough for about [140,000 treatment courses](#) (assuming a 10-day treatment course per patient). This stock is available for compassionate use, expanded access, clinical trials, and possibly other donations, although information regarding the countries eligible for these programmes remains unclear. The corporation stated that it takes six months to produce remdesivir, and that they aim to produce more than 500,000 treatment courses by October 2020, and more than one million treatment courses by the end of 2020. Following the emergency use approval by the US FDA, Gilead reported that a “donation” to the US government has been concluded and that [the allocation of 607,000 vials](#) of remdesivir for the US has begun. It is unclear how allocation to other countries will be determined and how the stock will be allocated within the US.

The corporation stated that they have repurposed some of their own manufacturing facilities to focus on the drug and are collaborating with contract manufacturers, increasing their “network of external manufacturing partners around the world,” and “building a geographically diverse consortium of pharmaceutical and chemical manufacturers to expand global capacity for raw materials and production.” However, no information about the actual agreements, nor the corporation’s engagement in licensing with generic companies, is available.

Gilead must disclose transparently its current manufacturing capacity. Gilead should also make the data required for regulatory purposes on remdesivir publicly available and share samples of the drug as required so that more manufacturers can produce remdesivir to ensure sustainable and timely supply worldwide.

Ensuring supply for low-resource settings and healthcare workers:

High-income countries must avoid overstocking or hoarding remdesivir, as this may limit its access in low-resource settings. Instead, a global coordination mechanism, led by the WHO, should be established to ensure that remdesivir is allocated based on public health and outbreak control needs, not the ability to pay high prices or the capacity to manufacture in-country.

If remdesivir is proven safe and effective, a network of manufacturers in different countries, including low- and middle-income countries, must be established and prepared for a rapid scale-up of supply. WHO and UN agencies should lead and coordinate an emergency preparedness and response mechanism to safeguard supplies to countries with weaker health systems and insufficient in-country manufacturing capacity.

Frontline healthcare workers in direct contact with people affected with this virus are at high risk. The availability of remdesivir for treatment of frontline healthcare workers must be guaranteed.

Tocilizumab

Overview

Roche and its subsidiary Genentech are the only global suppliers of tocilizumab, one of several potential treatments in the pipeline for COVID-19. The drug is being used in several countries for people with severe and critical cases of COVID-19, including in China, Italy, Spain and the US. The drug has been off-patent since 2017, but biosimilars are still under development.

To scale up production and ensure access, Roche/Genentech must disclose its manufacturing capacity and existing inventory and share its know-how, data and master cell line with any monoclonal antibody manufacturer, including existing developers of biosimilars of tocilizumab. Multiple sources of tocilizumab are needed to increase manufacturing capacity and decrease product price.

Medical and Clinical Trials

Tocilizumab is a monoclonal antibody therapy approved for the treatment of rheumatoid arthritis and the severe immune overreaction ('cytokine storm') caused by modern cancer treatments. The drug does not have any direct antiviral activity. Severe COVID-19 is characterised by a cytokine storm, which results in severe lung disease (acute respiratory distress syndrome [ARDS]). Tocilizumab may reverse the cytokine storm and ARDS not by direct action against the virus but by blocking interleukin-6 (IL-6), a substance produced by the body that boosts this exaggerated inflammatory response. Administered intravenously or subcutaneously, tocilizumab can be used in a single dose, and repeated one or two times if necessary.

A small observational study of 21 severe COVID-19 cases (including two critical cases) in Anhui, China reported a 100% discharge rate. A single-arm trial among critical patients with ARDS in Brescia, Italy (COMETA group) reported results from the first 100 patients, all with severe ARDS, with 77% improving or stabilising (a publication is expected in July 2020). French researchers at the National Institute of Health and Medical Research (INSERM) issued a press release with interim results from an open-label trial (CORUMINO) investigating different immunotherapies. Among 129 patients with moderate or severe COVID-19 pneumonia not requiring intensive care upon admission, a significantly lower proportion progressed to death or need for ventilation (non-invasive or mechanical). A publication on these results is currently in preparation; however, there are concerns regarding how the trial has been conducted, as evidenced by the resignation of the independent data monitoring committee following the publication of the press release.

Although the drug remains unapproved for the treatment of COVID-19, many cases have been treated off-label in different countries, with anecdotal reports and press releases showing promising results. Randomised clinical trials investigating the drug are under way in various countries. Although definitive results from randomised clinical trials published in peer-reviewed journals are not yet available, the drug seems promising.

A similar product, monoclonal antibody therapy sarilumab (Kevzara, manufactured by Sanofi/Regeneron), is being tested in a clinical trial in the US and Italy, against the cytokine storm, not specifically SARS-CoV-2 virus. Other host-targeted medications that work to alleviate the cytokine storm are being trialed as well.

Patents

The primary patent on tocilizumab expired in 2017. Several biosimilars are under development, but none have been approved by a regulatory authority, meaning that despite being off-patent, Roche/Genentech continue to have de facto market exclusivity on the drug. Secondary patents on the drug, and other types of market exclusivities, are also of concern, and may hinder access to this potentially key COVID-19 treatment.

Pricing

A single vial (400mg/20mL) of tocilizumab is needed to treat a person with COVID-19. The price of one vial of tocilizumab (400mg/20mL) produced by Roche/Genentech is between US\$400-800 in middle-income countries. The price may be higher in high-income countries. The costs to manufacture tocilizumab could be estimated to be as low as US\$40, given that the [manufacturing costs of monoclonal antibodies are often below US\\$100 per gram when produced on a large-scale](#). Roche/Genentech should agree to sell tocilizumab for COVID-19 at a much more affordable price than they currently do. In addition, Roche/Genentech should facilitate access to its know-how and master cell lines, so that more manufacturers are able to produce tocilizumab, and competition can bring down prices and increase patient access.

Supply

The demand for tocilizumab is expected to be high, should its efficacy demonstrated, with concerns that Roche/Genentech are unable to produce sufficient quantities of the drug to meet demand. Shortages are now reported in Spain and Ecuador. Roche/Genentech have donated vials of the drug to China, Italy, and Spain. The US Strategic National Stockpile acquired 10,000 doses on 23 March 2020, thus worsening the shortage crisis. On 28 March 2020, China announced it would donate 3,000 doses to Italy.

On supply and manufacturing, Roche/Genentech should take the following actions:

1. Disclose transparently its manufacturing capacity and existing inventory, and urgently scale up production.
2. Collaborate with additional manufacturers in high- and middle-income countries to quickly increase production in the short term.
3. Make publicly available its know-how, manufacturing secrets and master cell lines required to make the drug, so that manufacturers across the world can produce tocilizumab.

The development of biosimilars must also be expedited. There are several biosimilar candidates under development (in China, India, Switzerland, and Iran). They are not all at the same stage of development – some are at an advanced stage, but none have been approved. While these biosimilars were initially developed for rheumatoid arthritis, their repurposing for COVID-19 should be considered. Iran recently announced that its biosimilar version of tocilizumab is undergoing trials for COVID-19 and that its production can be scaled up.

Lopinavir/ritonavir (LPV/r)

Overview

Lopinavir/ritonavir (LPV/r), manufactured by pharmaceutical corporation AbbVie, is currently being tested and used in many countries against COVID-19. As the drug's primary indication is for HIV/AIDS (albeit not first choice for most patients but for specific situations), HIV advocacy groups are concerned that a surge in demand for LPV/r for COVID-19 treatment will negatively impact access to LPV/r for HIV/AIDS. The overall production and supply constraints of LPV/r could potentially result in shortages of LPV/r for the treatment of both COVID-19 and HIV/AIDS.

Although AbbVie has announced the non-enforcement of its patents on LPV/r worldwide, following a compulsory license issued by the Israeli government, supply concerns persist because of already ongoing shortages of the active pharmaceutical ingredients for this product, and generic companies have a limited capacity to increase supply.

Countries should refrain from irrational stockpiling or restricting export/import of pharmaceutical ingredients and finished products of LPV/r and should maintain international cooperation to ensure LPV/r is made available for people with HIV and according to public health need, ensuring supplies for countries with weaker health systems for both HIV/AIDS and COVID-19 treatment and prophylaxis if supported by clinical trial evidence.

Medical

There are now some reports that LPV/r is either ineffective for COVID-19 or poorly effective. A randomised clinical trial in China published in the *New England Journal of Medicine* did not find any benefit for LPV/r for severe (but not critical) patients compared to a control group (although it may still be useful if started earlier in the disease). A smaller randomised clinical trial in China of people with mild/moderate COVID-19 showed no benefit over the control or antiviral umifenovir (and a suggestion that the latter may be superior in preventing progression to severe disease). Another small study from China, an open-label non-randomised trial of mild/moderate patients, showed superiority of favipiravir over LPV/r (both combined with inhaled IFN-alpha) in terms of viral clearance and radiologic improvement. However, a recent randomised open-label multicentric phase II trial in Hong Kong of mild and moderate cases, published in *The Lancet*, showed reduced time for viral clearance (nasopharyngeal swabs - PCR) and clinical improvement when LPV/r was started early in the disease (up to seven days) combined with ribavirin and subcutaneous interferon beta-1b, as compared to LPV/r monotherapy. LPV/r alone and in combination with interferon are included in the ongoing WHO-sponsored randomised clinical trial (SOLIDARITY) taking place in different countries, including France, Germany, South Africa and Iran. Other HIV protease inhibitors antiretrovirals are also being tested in trials: *in vitro* action against SARS-CoV-2 was demonstrated for atazanavir but not darunavir. Pharmaceutical corporation Janssen has indicated that there is no evidence for the use of darunavir in SARS-CoV-2.

Patents

On 23 March 2020, compelled by a compulsory license issued by the Israeli government on LPV/r in order to secure access to an affordable generic version of the medicine, AbbVie announced its decision to not enforce any of its granted patents worldwide. While the removal of patents is one less hurdle to overcome, AbbVie's announcement should not be considered corporate philanthropy. AbbVie has a notoriously poor track record ensuring access to medicines. AbbVie's track record of undermining access to medicines include examples such as retaliation to Thailand in 2007 after the Thai government issued a compulsory license on LPV/r; and AbbVie's LPV/r voluntary licenses in 2015 with the Medicines Patent Pool (MPP), which did not cover the majority of middle-income countries where patents were a barrier (e.g. Ukraine and Malaysia), did not provide an adequate solution to enable access to LPV/r for people living with HIV. The long-term restriction and control by AbbVie over LPV/r have set the scene for the current global challenge of ensuring sufficient quantity of and accessibility to LPV/r.

Pricing

A recent pricing study estimated the manufacturing cost of LPV/r to be as low as [US\\$4](#) for a full treatment course, suggesting that this potential COVID-19 treatment could be made available to all at an affordable price during this pandemic.

Supply

The supply of LPV/r for people living with HIV is already extremely precarious. There is a global shortage for both the paediatric and adult formulations in the antiretroviral market which will be exacerbated by the stockpiling of LPV/r by countries for potential use in COVID-19.

Favipiravir

Medical

Favipiravir, produced by Fujifilm in Japan (originator manufacturer, brand name Avigan) and Hisun in China (generic manufacturer), is an oral antiviral drug used for years in Japan and other countries for influenza. It was tested against Ebola without positive results. Favipiravir has weak *in vitro* activity against SARS-CoV-2 and is currently recommended as an option for COVID-19 in Japanese guidelines. A small study from China, an open-label non-randomised trial of

mild/moderate patients, showed superiority of favipiravir over LPV/r (both combined with inhaled IFN-alpha) in terms of viral clearance and radiologic improvement. A larger trial compared favipiravir with antiviral umifenovir and showed a slightly shorter time to improvement for some symptoms and, among moderate cases, a lower risk of deterioration. However, another small exploratory trial (preprint) showed no benefit when compared to baloxavir or the control and showed that it wasn't possible to achieve a sufficient concentration of favipiravir in the blood (enough to kill SARS-CoV-2). There are concerns of teratogenicity, which has been seen in animal species studied: both female and male patients treated with favipiravir should be asked to implement strict contraception up to seven days after treatment. There are several generic companies in India working on this product including [Aurobindo](#), [Cipla](#), [Mylan](#) and [Dr Reddy's Lab](#).

Patents

The primary patent for favipiravir expired in 2019.

Pricing

Fujifilm sells favipiravir at around US\$3 per tablet. The price of a full treatment course (assuming a dosage of 600mg twice a day for 14 days) is therefore US\$252. According to a [recent pricing](#) study, the manufacturing costs of a full treatment course may be as low as US\$20, suggesting that this potential COVID-19 treatment could be made available to all at an affordable price during this pandemic.

Supply

Hisun's generic version of favipiravir has been approved by the Chinese FDA for the treatment of influenza and is being used off-label for COVID-19. The company is undertaking supplementary studies to register the drug for the new indication of COVID-19. Registration information in other countries is pending.

Manufacturers in India and Bangladesh have recently announced that they expect to be able to manufacture generic favipiravir within a few weeks.

Fujifilm have stocks of the drug and capacity to increase production. The drug is registered in Japan for the treatment of influenza. MSF could use the drug under 'compassionate use' or clinical trial conditions. Fujifilm is cautious about which countries they send the drug to, and they need to ensure it is not used in pregnant women. The Japanese government appears willing to collaborate with other countries to conduct clinical trials and increase production. The Japanese government has received about 50 requests from other governments and has since arranged for a donation, the logistics of which will be managed by United Nations Office for Project Services (UNOPS), to allocate the drug among countries in alignment with guidance for use by WHO.

SUMMARY TABLE

Access issues for selected candidate therapeutics for COVID-19*

Colour code:

- **Green**: Sufficient
- **Yellow**: Of concern
- **Red**: Critical (lacking access guarantees)

Drug	Price (USD)	Supply & Capacity	Intellectual Property Barriers	Regulatory Challenges
Favipiravir (FPV) tablets	Estimated cost to manufacture as low as \$1.45 per day, \$20 per treatment Price from FujiFilm is \$3 per tablet,	Japan stockpiling enough for 2 million treatments Company increasing production to 100,000 treatments (14 days) by July 2020 and 300,000 by Sept 2020	No longer patented Secondary patent for indication of COVID-19 may be problematic in some countries	Approved in Japan for influenza Regulatory approval for new indication may lead to new exclusivities for a limited period of time in some countries

	\$252 per treatment	20-100 treatments per country being supplied to about 50 countries via UNOPS One generic supplier in China and multiple in development in India		
Lopinavir/ritonavir (LPV/r) tablets	Global Fund price in HIV market: \$9 per treatment <u>Estimated</u> cost to manufacture as low as \$0.28 per day, \$4 per treatment	Despite multiple generics, HIV market facing global shortage, which would be exacerbated if countries stockpile or block export of LPV/r for COVID-19.	Abbvie <u>relinquished patents</u> globally	Approved globally for use in HIV treatment Regulatory approval for new indication may lead to new exclusivities for a limited period of time in some countries
Remdesivir (RDV) vials	Gilead's price unknown ICER estimates <u>\$4,460 per treatment</u> Estimated cost to manufacture as low as <u>\$0.93 per day</u> , \$9 per treatment	Gilead <u>donated >140,000 treatment courses</u> of RDV to the US, said they will produce 1 million treatment courses by end 2020 Multiple generic manufacturers developing RDV	Gilead filed patents in <u>>79 countries</u> until 2031 Concluded <u>negotiations</u> for voluntary licensing with five generic companies in India and Pakistan to supply 116 countries and 11 territories; excluded most Latin American countries, China, Russia, and Malaysia, among other LMICs	Authorized for emergency use in US; approved in Japan and UK; under rolling review by the European Medicines Agency
Tocilizumab, 400mg/20ml vials	<u>Estimated</u> cost to manufacture unknown Potentially <\$40 for a 400mg vial, given cost <u>of <\$100</u> per g for same product category Priced at \$400-800 per 400 mg vial in MICs	Limited supply available from Roche/Genentech (sole supplier) No biosimilar yet approved but several in development	Primary <u>patents</u> expired Secondary patents may block biosimilar use in some countries	Approved for use in rheumatoid arthritis and cytokine storm associated with cancer therapy Regulatory approval for new indication may lead to new exclusivities for a limited period of time in some countries

UNOPS = United Nations Office for Project Services; LMIC = low- or middle-income country; MIC = middle-income country

*Disclaimer: The drugs selected here for analysis are in various stages of clinical trials. The information provided is being updated on a regular basis but may not be completely up to date due to rapid developments. Please refer to the last updated date at the beginning of the document.