

# **Potential medicines to treat COVID-19**

**17 April 2020**

## Potential medicines to treat COVID-19

SARS-CoV-2 is a novel coronavirus that causes the illness COVID-19. There are no approved medicines to treat COVID-19 and no vaccine is available. Most treatments focus on symptom relief. Oxygen therapy represents the major treatment intervention for patients with severe infection. Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy. Hemodynamic support is essential for managing septic shock.

The following sections summarise medicines being investigated to treat COVID-19. Medicines where there is emerging evidence against COVID-19 are described. There is a lack of robust evidence on specific treatment options for COVID-19 and any proposed therapies are considered experimental at this stage. Some are included in clinical trial research.

The emphasis of investigation of potential treatments for COVID-19 has focussed on repurposing existing medicines<sup>1</sup> For example, lopinavir / ritonavir and chloroquine.<sup>2,3</sup>

The [SOLIDARITY trial](#) was launched by the World Health Organization on 20 March 2020. It is an international clinical trial of four treatment options assessing effectiveness against COVID-19. The trial aims to reduce clinical trial investigation time by 80% by recruiting many countries in a single study of scale to generate data in a short time.

In Australia, on 30 March 2020 it was announced that the Peter Doherty Institute for Infection and Immunity at the University of Melbourne received funding to work on the ASCOT trial. Specifically, lopinavir-ritonavir and hydroxychloroquine will be assessed in patients with COVID-19, admitted to hospital but not to an ICU in 60 hospitals across Australia over the next 2 months.<sup>4</sup>

Due to the rapidly evolving nature of the COVID-19 pandemic, and the number of papers being prepared to share findings, many references have not been peer-reviewed. Their purpose is to allow other scientists to see, discuss, and comment on the findings immediately. Such preprints are yet to be evaluated by the medical community and the information presented may be erroneous. This should be acknowledged when considering options for application in clinical practice.

Work is ongoing to fact check and build on the entries for each medicine. To support this work, the Commission will seek expert opinion from within Australia, for example in pharmacology, epidemiology and virology. The Commission is supported across programs by an extensive network of experts and stakeholders, including peak bodies and universities. Specifically, for medication safety this includes the Health Services Medication Expert Advisory Group that meets quarterly and includes members from all States and Territories. The Commission expects to consult with these organisations to assist with development of resources to support the areas described here.

Managing medicines in patients with COVID-19, outside of investigating experimental treatments is considered in a set of position statements under consultation and reviewed regularly at [Medicines management COVID-19](#).

## Monoclonal antibodies

### Tocilizumab (Actemra®)

Australian sponsor	Roche Products Pty Ltd
Australian status	TGA registered
PBS listing	<a href="#">Yes</a>
Sponsor information	<a href="#">Roche, Actemra</a>
Prescribing information	<a href="#">TGA</a>
	<a href="#">Guildlink</a>
	<a href="#">Complications</a>

Tocilizumab (Actemra) is a biologic medicine indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients with poor prognostic factors in combination with methotrexate (MTX) or other non-biological disease-modifying anti-rheumatic drugs (DMARDs).

In 2010, Actemra secured approval from the US Food and Drug Administration (FDA) for the treatment of rheumatoid arthritis (RA). The drug is capable of inhibiting high Interleukin 6 (IL-6) protein levels. This is a pro-inflammatory cytokine implicated in some inflammatory diseases.

China's National Health Commission in treatment guidelines published online, indicated Actemra may be used to treat coronavirus patients with severe lung damage and high IL-6 levels. Researchers in China are expected to enrol a total of 188 patients with COVID-19 in a clinical trial running through to 10 May 2020.<sup>5,6</sup>

Actemra does not directly kill the novel coronavirus, known as SARS-CoV-2. In the disease COVID-19, the body may respond to the pathogen by overproducing immune cells and their signalling molecules in a dangerous phenomenon called a cytokine storm. Similar lung inflammation happened in SARS patients during the 2003 outbreak, mainly in China. It is hypothesised that Actemra may have potential against this activity as an inhibitor of the interleukin 6 (IL-6) receptor.

### **Sarilumab (Kevzara®)**

Australian sponsor	Sanofi-Aventis Australia Pty Ltd
Australian status	TGA registered
PBS listing	No ( <a href="#">Public summary document 1 March 2019</a> )
Prescribing information	<a href="#">TGA</a>
	<a href="#">Injection</a>
	<a href="#">Locations</a>

Sarilumab (Kevzara) is an IL-6 inhibitor that in combination with non-biological Disease-Modifying Anti-Rheumatic Drugs (DMARDs) or as monotherapy is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have had an inadequate response or intolerance to one or more DMARDs.

Kevzara was approved by the FDA in 2017. Sanofi-Aventis development partner, Regeneron is planning a clinical trial in severe/critical COVID-19 patients to evaluate Sarilumab. The trial is based on findings from China with another IL-6 inhibitor that showed a benefit in reducing fever and increasing lung capacity in severe and critical hospitalised patients with COVID-19.

Regeneron is also pursuing further clinical tests of an antibody, potentially finding a use as a prophylaxis in first responders and healthcare workers as a stand-alone treatment or as a combo with Kevzara.

### **Meplazumab**

Australian sponsor	To be determined
Australian status	Not registered
Approach	Treatment

Stage: To evaluate the safety and efficacy of humanized Meplazumab for Injection in patients infected by 2019-nCoV – ClinicalTrials.gov Identifier: NCT04275245

A trial in China in February 2020<sup>7</sup> aimed to assess the efficacy and safety of meplazumab, a humanized anti-CD147 antibody, as add-on therapy in patients with COVID-19 pneumonia. It has been proved that host-cell-expressed CD147 could bind the spike protein of SARS-CoV-2 involved in host cell invasion. Antibody against CD147 could block the infection of SARS-CoV-2. The authors interpreted that meplazumab efficiently improved the recovery of patients with SARS-CoV-2 pneumonia with a favourable safety profile. They support further large-scale investigation of meplazumab as a treatment for COVID-19 pneumonia.

### Monoclonal Antibodies unspecified

Australian sponsor	To be determined
International sponsor	Vir Biotechnology
Approach	Treatment
Stage	Preclinical

Vir Biotechnology has isolated antibodies from people who survived Severe Acute Respiratory Syndrome (SARS), a viral relative of the novel coronavirus COVID-19. Vir has identified a number of monoclonal antibodies that bind to SARS-CoV-2, which were isolated from individuals who had survived a SARS infection. Research continues to determine if its antibodies, or additional antibodies that it may be able to identify, can be effective as treatment and/or prophylaxis against SARS-CoV-2.<sup>8</sup>

WuXi Biologics in partnership with Vir is in the early stages of development and has not specified when it expects to have products ready for human testing.<sup>9</sup>

## Antiretrovirals

### Lopinavir / ritonavir (Kaletra®)

Australian sponsor	AbbVie Pty Ltd
Australian status	TGA – combination registered
PBS listing	<a href="#">Yes</a>
Indication	For the treatment of HIV-1 infection, in combination with other antiretroviral agents in adults and children aged 2 years and older
Prescribing information	<a href="#">TGA</a>

Lopinavir and ritonavir inhibit protease, an enzyme that HIV and coronaviruses use to replicate.

In January 2020, AbbVie donated a supply of lopinavir / ritonavir to the Chinese health authorities for use as an experimental treatment option.<sup>10</sup> AbbVie's fixed-dose HIV drug Kaletra, a combination of antivirals lopinavir and ritonavir, was trialled in January 2020 in Wuhan with the published results concluding no improvement in clinical symptoms, extension of lifespan or cutting viral shedding in patients hospitalised with severe COVID-19.<sup>11</sup> In further analysis a mortality benefit was reported for patients who received Kaletra earlier. The death rate in Kaletra patients was 15.0% at day 28, versus 27.1% among placebo patients, provided therapy started within 12 days of showing symptoms.<sup>12</sup>

### **Darunavir / Cobicistat (Prezcobix®)**

Australian sponsor	Janssen-Cilag Pty Ltd
Australian status	TGA registered
PBS listing	<a href="#">Yes</a>
Indication	In combination with other antiretroviral agents for the treatment of adult patients with human immunodeficiency virus1 (HIV-1) infection
Prescribing information	<a href="#">TGA</a>

There are several classes of drugs in development, including antivirals, immunotherapies, and vaccines. It is unknown whether a single drug could work or if a combination is needed. Prezcobix used to treat HIV infections is under investigation.<sup>13</sup>

Janssen has donated 300 boxes of its HIV medicine darunavir/cobicistat to the Shanghai Public Health Clinical Center and Zhongnan Hospital of Wuhan University to support research into a solution for the SARS-CoV-2. Another 50 boxes have been provided to the Chinese Centre for Disease Control and Prevention for laboratory-based drug-screening for antiviral properties against SARS-CoV-2.<sup>14</sup> More recently, Johnson & Johnson announced that there have been anecdotal and unsubstantiated reports that darunavir marketed by its company Janssen as Prezista / Prezcobix is being used in treatment. However, there is no evidence of any effect against SARS-CoV-2.<sup>15</sup>

## **Antivirals**

### **Umifenovir (Arbidol®)**

Australian sponsor	Not identified
Australian status	TGA – not registered

Arbidol is the trade name for umifenovir, a non-nucleoside antiviral and immunomodulating drug. The influenza remedy Arbidol (umifenovir) is not approved in Western countries but has been approved for use in China.

Umifenovir was first developed in the Russian Research Chemical-Pharmaceutical Institute in the late 1980s. In 2006, Arbidol was approved for the treatment of upper respiratory tract infections caused by influenza virus A and B in adults by the China Food and Drug Administration.<sup>16</sup>

In March 2020, an interventional planned Phase IV trial at Xiang Hospital of central South University in Hunan province in China, aimed to recruit 500 patients to investigate the use of umifenovir as an add-on to antiviral combination therapy. The trial is split into three arms. The two experimental arms study the administration of 200mg and 400mg of umifenovir respectively, alongside control arm of conventional antiviral therapy in the treatment of coronavirus.<sup>17</sup>

In Russia and China, umifenovir is widely used as a prophylactic against and treatment for colds with hundreds of millions of doses sold per year. While there is evidence that it has antiviral properties, its effectiveness has been disputed in some trials, and it is not approved for use in the EU or the US.

The UK Medicines and Healthcare Regulatory Agency (MHRA) confirmed that the Arbidol being sold on eBay UK and other websites “is not licensed for sale in UK”. The MHRA note that while some drugs can be legally sold online by registered pharmacists, “many websites are operating illegally, there are no qualified healthcare providers involved in the supply and the medicines supplied may not be the authorised product”.<sup>18</sup>

## **Remdesivir**

Australian sponsor (likely)	Gilead Sciences Pty Ltd
Australian status	TGA – not registered

Remdesivir is an investigational nucleotide analogue originally developed for Ebola. It is not approved anywhere globally and has not been demonstrated to be safe or effective for any use.<sup>19</sup>

Remdesivir has demonstrated broad-spectrum antiviral activity both in vitro and in animal models against multiple emerging viral pathogens including Marburg, MERS, SARS, and more recently Ebola. The viral pathogens MERS and SARS are also coronaviruses and are structurally similar to the SARS-CoV-2 that causes COVID-19. The limited preclinical data for remdesivir in MERS and SARS indicates that the medicine may have potential activity against SARS-CoV-2.

In March 2020, Gilead commenced a phase 3 studies of remdesivir in adults diagnosed with COVID-19 to evaluate the safety and efficacy. These randomised, open-label, multicentre studies aim to enrol approximately 1,000 patients at medical centres primarily across Asian countries, as well as other countries globally with high numbers of diagnosed cases. The trial aims to determine whether multiple doses of remdesivir can reverse the infection. The primary goals are reducing fever and helping patients discharge from hospital within two weeks. Gilead’s remdesivir, an intravenous treatment, has been used to treat one infected patient in the US.<sup>20</sup>

These studies complement those being undertaken by the National Institute of Allergy and Infectious Diseases (NIAID) in the US, and others being conducted in China led by the China-Japan Friendship Hospital.<sup>21</sup>

On 27 March 2020, the WHO announced that in Norway and Spain, the first patients will be enrolled in the SOLIDARITY trial. SOLIDARITY will compare the safety and effectiveness of four different medicines or medicine combinations against COVID-19: remdesivir; chloroquine and hydroxychloroquine; lopinavir plus ritonavir; and lopinavir plus ritonavir and interferon-beta.

More than 90 countries are contributing to the trial, and more have expressed interest. The high numbers are expected to dramatically cut the time needed to generate robust evidence about what drugs are effective.<sup>22</sup>

On 1 April 2020, Gilead Sciences announced the initiation of two phase 3 randomised studies to evaluate the safety and efficacy of its investigational treatment remdesivir in patients with moderate to severe COVID-19. The two studies which have been given urgent public health research (UPHR) status by the Chief Medical Office will initially involve 15 centres in the UK.



### **Favipiravir (Avigan®)**

Australian sponsor (likely)	FUJIFILM Toyama Chemical Co. Ltd
Australian status	TGA – not registered

Favipiravir is a broad-spectrum antiviral originally developed for influenza and also tested against Ebola virus disease. After oral absorption, it is converted into a bioactive nucleoside triphosphate compound that shares a similar structure with purine and competes with purine to inhibit RNA polymerase and block virus replication.

China now has six clinical trials investigating favipiravir. Sihuan Pharmaceutical Holdings Group Ltd. said it has initiated clinical trials of broad-spectrum antiviral favipiravir to treat COVID-19. According to the Chinese Clinical Trial Registry, it is a randomized, open-label, controlled trial to investigate the efficacy and safety of favipiravir. Low, middle and high dosage groups will each see 20 patients receive favipiravir twice a day at 1,600 mg, 1,800 mg and 2,400 mg, respectively, for 10 days. The clinical trial was registered on 20 February 2020.<sup>23</sup>

In Japan, favipiravir was developed as an anti-influenza medication by Toyama Chemical Co. Ltd., a division of Fujifilm. Avigan was approved in Japan in March 2014 to treat influenza in patients who do not respond to other therapies. On 22 February 2020, Katsunobu Kato, Japan's Minister of Health, Labor and Welfare, said the country is planning to test Fujifilm's favipiravir against the coronavirus.

Although Avigan has not been approved by the South Korean government, South Korea's Ministry of Food and Drug Safety also said on 25 February 2020 that it is considering fast-track approval to import Avigan for the treatment of COVID-19.<sup>24</sup>

## **Antimalarials**

### **Chloroquine (Chlorquin™)**

Australian sponsor	Aspen Pharmacare Australia Pty Ltd
Australian status	TGA registered
PBS listing	No
Indication	Treatment of malaria

Chloroquine blocks viral infection by increasing endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV.<sup>25</sup>



## Hydroxychloroquine (Plaquenil®)

Australian sponsor	Sanofi-Aventis Australia Pty Ltd
Australian status	TGA registered
PBS listing	<a href="#">Yes</a>
Indication	Rheumatoid arthritis; mild systemic and discoid lupus erythematosus; the suppression and treatment of malaria
Prescribing information	<a href="#">TGA</a>

Yao et al<sup>26</sup> found hydroxychloroquine to be more potent than chloroquine to inhibit SARS-CoV-2 in vitro.

Gautret et al<sup>27</sup> published the results in March 2020 of an open-label non-randomised clinical trial using hydroxychloroquine and azithromycin as a treatment for COVID-19. The authors concluded that hydroxychloroquine treatment is significantly associated with viral load reduction / disappearance in COVID-19 patients and its effect is reinforced by azithromycin. This paper attracted much attention – criticism that it was published before a meaningful endpoint was reached and conclusions were drawn on a small sample size. However, there was support for raising awareness of the prospects for hydroxychloroquine.

Considerable media attention on anti-malarial medicines with potential to treat COVID-19 has seen increased demand, especially for chloroquine and hydroxychloroquine. The FDA has not approved these medicines to treat COVID-19.

In response to off-label use in Australia, the Therapeutic Goods Administration (TGA) on 24 March 2020 introduced new restrictions on who can initiate therapy with hydroxychloroquine in unapproved indications. Only the following medical specialties will be able to prescribe: dermatology, intensive care medicine, paediatrics and child health, physician, and emergency medicine.<sup>28</sup>

On 30 March 2020, a group of academic colleges (American Academy of Dermatology, American College of Rheumatology) and associations of disease states (Lupus Foundation of America, Arthritis Foundation) wrote to US Vice President Pence, urging collaboration to ensure the continued availability of chloroquine and hydroxychloroquine for patients with lupus and rheumatoid arthritis who are maintained on them to avoid disability, illness and early death.<sup>29</sup>

On 31 March 2020, a study by Chen et al<sup>30</sup> concluded that among patients with COVID-19, the use of hydroxychloroquine could significantly shorten time to clinical recovery (TTCR) and promote the absorption of pneumonia. Between the control group and the hydroxychloroquine group, the body temperature recovery time and the cough remission time were significantly shortened in the hydroxychloroquine treatment group.

## **Antimicrobials / Antiseptics / Antinematodal agents**

In March 2020, Poschet et al<sup>31</sup> reported that azithromycin and ciprofloxacin have a chloroquine-like effect on respiratory epithelial cells. They report that azithromycin and ciprofloxacin (as has been previously demonstrated for chloroquine) alter the pH within the intracellular organelles in respiratory epithelial cells. This correction results in a normalisation of the cell-autonomous immune functions of respiratory epithelia in CF. There is a suggestion that the actions of azithromycin and ciprofloxacin's action may overlap with chloroquine's mode of action and propose clinical trials with patients at risk of developing severe COVID-19.

### **Azithromycin (Zithromax®)**

Australian sponsor	Pfizer Australia Pty Ltd
Australian status	TGA registered
PBS listing	<a href="#">Yes</a>
Indication	Antibacterial
Prescribing information	<a href="#">TGA</a>

Azithromycin is indicated for use in adults for the treatment of the following infections of mild to moderate severity, and is used for lower respiratory infections such as:

- Acute bacterial bronchitis due to *Streptococcus pneumoniae*, *Haemophilus influenzae* or *Moraxella catarrhalis*.
- Community acquired pneumonia due to *Streptococcus pneumoniae* or *Haemophilus influenzae* in patients suitable for outpatient oral treatment.
- Community acquired pneumonia caused by susceptible organisms in patients who require initial intravenous therapy.

In clinical studies efficacy has been demonstrated against *Chlamydia pneumoniae*, *Haemophilus influenzae*, *Legionella pneumophila*, *Moraxella catarrhalis*, *Mycoplasma pneumoniae*, *Staphylococcus aureus* and *Streptococcus pneumoniae*.

Azithromycin is also used for upper respiratory infections such as acute sinusitis due to *Streptococcus pneumoniae* or *Haemophilus influenzae* and acute Streptococcal pharyngitis.

## Ciprofloxacin

Australian sponsor	Bayer Australia Ltd
Originator brand	Ciproxin®
Australian status	TGA registered
PBS listing	<a href="#">Yes</a>
Indication	Antibacterial
Prescribing information	<a href="#">TGA</a>

The bactericidal action of ciprofloxacin appears to result from interference with the enzyme, DNA gyrase, with activity against a wide range of Gram-negative and Gram-positive organisms.

## Povidone-iodine

Australian sponsor	Sanofi-Aventis Australia Pty Ltd
Originator brand	Betadine®
Australian status	TGA registered
PBS listing	Betadine Ready to Use Sore Throat Gargle: No Betadine Antiseptic Topical Solution: <a href="#">Yes</a> – Repeat only
Indication	Antiseptic/disinfectant
Prescribing information	<a href="#">TGA</a>

The use of povidone-iodine gargle is well established. In 2002, Shiraishi T et al<sup>32</sup> published results of a study to compare the bactericidal activities of a povidone-iodine (PVP-I) gargle with those of other commercially available gargles containing chlorhexidine gluconate (CHG) and cetylpyridium chloride (CPC). In vivo, with subjects in groups of 6 each, the reduction rate in the oral bacterial count after gargling as compared to the baseline count before gargling was determined and compared among the 3 gargling agents used. The authors concluded that of the 3 gargles tested, PVP-I showed the highest bactericidal rate and the highest reduction rate in oral bacterial count. They also investigated whether the encouragement to use the PVP-I gargle had an effect on the absence rate from middle school due to common cold and influenza. They concluded that encouraging the use of the PVP-I gargle contributed to the decrease in absence rates due to common cold and influenza.

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In 2013<sup>33</sup>, a study on *in vitro* bactericidal and virucidal efficacy of povidone-iodine (PVP-I) 7% gargle/mouthwash at defined dilution (equivalent to a concentration of 0.23% PVP-I) against oral and respiratory tract pathogens showed effective bactericidal activity against *Klebsiella pneumoniae* and *Streptococcus pneumoniae*. It also rapidly inactivated SARS-CoV, MERS-CoV, influenza virus A (H1N1) and rotavirus after 15 seconds of exposure. The authors concluded that povidone-iodine gargle / mouthwash may provide a protective oropharyngeal hygiene measure for individuals at high risk of exposure to oral and respiratory pathogens.

In 2015, Eggers M et al<sup>34</sup> published results of the virucidal activity of povidone-iodine against Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The authors concluded that povidone-iodine gargle / mouthwash for reduction of viral load in the oral cavity and the oropharynx may help to support hygiene measures to prevent transmission of MERS-CoV.

In a study published in 2018<sup>35</sup>, the authors concluded that a povidone-iodine 7% gargle/mouthwash showed rapid bactericidal activity and virucidal efficacy *in vitro* at a concentration of 0.23% PVP-I and may provide a protective oropharyngeal hygiene measure for individuals at high risk of exposure to oral and respiratory pathogens.

Povidone iodine topical solution is included in the World Health Organization's list of essential medicines<sup>36</sup>. The high potency of povidone-iodine for virucidal activity has been observed against viruses including hepatitis A and influenza, as well as MERS-CoV and SARS-CoV coronaviruses.<sup>37</sup>

### Ivermectin

Australian sponsor	Merck Sharp & Dohme Pty Ltd
Originator brand	Stromectol®
Australian status	TGA registered
PBS listing	<a href="#">Yes</a>
Indication	Onchocerciasis, Strongyloidiasis, crusted scabies, human sarcoptic scabies (Authority required)
Prescribing information	<a href="#">TGA</a>

A collaborative study published on 3 April 2020 has shown that the anti-parasitic drug, ivermectin stopped the SARS-CoV-2 virus growing in cell culture within 48 hours.<sup>38</sup> The study is led by the Monash Biomedicine Discovery Institute (BDI) with the Peter Doherty Institute of Infection and Immunity (Doherty Institute), a joint venture of the University of Melbourne and Royal Melbourne Hospital. While ivermectin is widely used with a well-documented safety profile, investigators cautioned that they need to establish if the dosage that can be used safely in humans will be effective to treat those with COVID-19.

Ivermectin improved the nutrition, general health and wellbeing of billions of people worldwide ever since it was first used to treat onchocerciasis in humans in 1988. It is highly effective, has a broad spectrum of activity, is well tolerated and could be easily administered via a single, annual oral dose. It is used to treat a variety of internal nematode infections including onchocerciasis, strongyloidiasis, ascariasis, cutaneous larva migrans, filariases, gnathostomiasis and trichuriasis. It is also used as oral treatment of ectoparasitic infections, such as pediculosis (lice infestation) and scabies (mite infestation).<sup>39</sup>

## Others

### Melatonin

Australian sponsor	RAD Data Australia Pty Ltd
Originator brand	Circadin®
Distributed by	Aspen Pharmacare Australia Pty Ltd
Australian status	TGA registered
PBS listing	No
Indication	Monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over

Zhang et al<sup>40</sup> propose that excessive inflammation, oxidation, and an exaggerated immune response likely contribute to COVID-19 pathology. This is based on clinical features, pathology and the pathogenesis of acute respiratory disorder induced by coronaviruses or other pathogens. They suggest this leads to a cytokine storm and subsequent progression to acute lung injury (ALI) / acute respiratory distress syndrome (ARDS) and often death. Melatonin, is an anti-inflammatory and anti-oxidative molecule, and the authors suggest it may be protective against ALI / ARDS caused by viral and other pathogens. The authors also note that melatonin is effective in critical care patients by reducing vessel permeability, anxiety, sedation use, and improving sleeping quality.

### Chlorpromazine

Australian sponsor	Sanofi-Aventis Australia Pty Ltd
Originator brand	Largactil®
Australian status	TGA registered
PBS listing	<a href="#">Yes</a>
Indication	Antipsychotic
Prescribing information	<a href="#">TGA</a>

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Chlorpromazine is used to treat acute functional psychosis (e.g. schizophrenia, mania or psychotic depression), long-term treatment of schizophrenia, short-term treatment of agitation and severe depression. It is also used in terminal illness management to enhance the effect of analgesics and control nausea, vomiting, and intractable hiccough.

Yang et al<sup>41</sup> reviewed the endocytic pathway and autophagy process in viral infection of several pathogenic coronaviruses including SARS-CoV, MERS-CoV and the new SARS-CoV-2. They discuss the development of therapeutic agents targeting these processes and concluded that the exact role of autophagy is debatable. However, evidence suggests that the endocytic pathway plays a role in mediating viral entry for many coronaviruses, including SARS-CoVs, and possibly SARS-CoV-2. As a result, several inhibitors targeting the endocytic pathway appear to have the therapeutic potential in treatment of COVID-19, including a lysosomotropic agent, chloroquine and a clathrin-mediated endocytosis inhibitor, chlorpromazine. The authors call for clinical trials either as a single therapy or in combination with other anti-viral drugs as the medicines are already FDA approved.

## Further resources and treatment summaries

[The Australian Department of Health off-label medicines advice for treatment and prophylaxis of COVID-19<sup>42</sup>](#)

[UK guidelines for the use of medicines in COVID-19 \(D20-8578\)](#)

[American Society of Hospital Pharmacists: Assessment of Evidence for COVID-19-Related Treatments](#)

[The Council of Australian Therapeutic Advisory Groups \(CATAG\) position on Antiviral treatment of COVID-19<sup>43</sup>](#)

[The Centre for Communicable Diseases in the US drug treatment guidelines](#)

[National Institutes of Health – COVID-19 latest research information](#)

[Elsevier COVID-19 Drug Therapy](#)

[Medscape Coronavirus Disease 2019 \(COVID-19\) Treatment & Management](#)

[Drug Virus information](#)

[National COVID-19 Clinical Evidence Taskforce](#)

[International Union of Basic and Clinical Pharmacology \(IUPHAR\) / British Pharmacological Society \(BPS\) Guide to Pharmacology](#)

[COVID-19 Pharmacology Resource Center](#)

[Australian Medical Association \(AMA\) COVID-19 Pharmacologic Treatment](#)



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