



# Drug Information Bulletin

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## *Editorial*

*This is a critical and difficult time when I am writing this editorial. India is reeling under the threat of Phase-3 of Corona virus epidemic/Pandemic.*

*As per WHO update today 308547 COVID-19 cases have been found, 13069 deaths have occurred globally, whereas 95829 have recovered. In India 332 cases have been identified and 5 death cases reported, whereas 24 patients have recovered. Till today Indian situation is comparatively better than some other countries, but India is entering to the third phase from 23 rd march which is the more dangerous and crucial infectious phase. In the mean time central and state governments have already taken serious precautionary measures to prevent spreading this infection and breaking their chain of transmission. To ensure availability of masks and hand sanitizers they have taken double pronged approach-*

- 1. Increasing availability of these two items by arranging more production.*
- 2. Improving availability by preventing hoarding and imposing price control.*

*Awareness campaign by the health authorities of this country is highly appreciable.*

*We must support all health care personnel who are working 24X7 to take care of the situation*

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## Information for Clinicians on Therapeutic Options for COVID-19 Patients

At present clinical management of COVID-19 includes infection prevention and control measures and supportive care, including supplementary oxygen and mechanical ventilator support when indicated. An array of drugs approved for other indications as well as several investigational drugs are being studied in several hundred clinical trials that are underway across the globe. The purpose of this document is to provide information on two of the approved drugs (Chloroquine and Hydroxychloroquine) and one of the investigational agents (remdesivir) currently in use in the United States.

### Remdesivir

Remdesivir is an investigational intravenous drug with broad antiviral activity that inhibits viral replication through premature termination of RNA transcription and has in-vitro activity against SARS-CoV-2 and in-vitro and in-vivo activity against related betacoronaviruses <sup>[1-3]</sup>.

There are currently four options for obtaining remdesivir for treatment of hospitalized patients with COVID-19 and pneumonia in the United States:

- A National Institutes of Health (NIH)-sponsored adaptive double-blinded, placebo-controlled trial of remdesivir versus placebo in COVID-19 patients with pneumonia and hypoxia is enrolling non-pregnant persons aged 18 years and older with oxygen saturation of  $\leq 94\%$  on room air or requiring supplemental oxygen or mechanical ventilation (<https://clinicaltrials.gov/ct2/show/NCT04280705> [external icon](#)). Exclusion criteria include alanine aminotransaminase or aspartate aminotransaminase levels  $>5$  times the upper limit of normal, stage 4 severe chronic kidney disease or a requirement for dialysis (i.e., estimated glomerular filtration rate (eGFR)  $<30$ );
- Two phase 3 randomized open-label trials of remdesivir (5-days versus 10-days versus standard of care) are open to enrollment in persons aged 18 years and older with COVID-19, radiographic evidence of pneumonia and

oxygen saturation of  $\leq 94\%$  on room air (severe disease <https://clinicaltrials.gov/ct2/show/NCT04292899> [external icon](#)) or  $>94\%$  on room air (moderate disease <https://clinicaltrials.gov/ct2/show/NCT04292730> [external icon](#)). Exclusion criteria include alanine aminotransaminase or aspartate aminotransaminase levels  $>5$  times the upper limit of normal, participation in another clinical trial of an experimental treatment for COVID-19, requirement for mechanical ventilation, or creatinine clearance  $<50$  mL/min; and

- Finally, in areas without clinical trials, COVID-19 patients in the United States and other countries have been treated with remdesivir on an uncontrolled compassionate use basis. While clinical trials are critical to establish the safety and efficacy of this drug, clinicians without access to a clinical trial may request remdesivir for compassionate use through the manufacturer for patients with clinical pneumonia: [compassionateaccess@gilead.com](mailto:compassionateaccess@gilead.com)

### Hydroxychloroquine and Chloroquine

Hydroxychloroquine and chloroquine are oral prescription drugs that have been used for treatment of malaria and certain inflammatory conditions. Chloroquine has been used for malaria treatment and chemoprophylaxis, and hydroxychloroquine is used for treatment of rheumatoid arthritis, systemic lupus erythematosus and porphyria cutanea tarda. Both drugs have in-vitro activity against SARS-CoV, SARS-CoV-2, and other coronaviruses, with hydroxychloroquine having relatively higher potency against SARS-CoV-2 <sup>[1,4,5]</sup>. A study in China reported that chloroquine treatment of COVID-19 patients had clinical and virologic benefit versus a comparison group, and chloroquine was added as a recommended antiviral for treatment of COVID-19 in China <sup>[6]</sup>. Based upon limited in-vitro and anecdotal data, chloroquine or hydroxychloroquine are currently recommended for treatment of hospitalized COVID-19 patients in several countries. Both chloroquine and hydroxychloroquine have known

safety profiles with the main concerns being cardiotoxicity (prolonged QT syndrome) with prolonged use in patients with hepatic or renal dysfunction and immunosuppression but have been reportedly well-tolerated in COVID-19 patients.

Due to higher in-vitro activity against SARS-CoV-2 and its wider availability in the United States compared with chloroquine, hydroxychloroquine has been administered to hospitalized COVID-19 patients on an uncontrolled basis in multiple countries, including in the United States. One small study reported that hydroxychloroquine alone or in combination with azithromycin reduced detection of SARS-CoV-2 RNA in upper respiratory tract specimens compared with a non-randomized control group but did not assess clinical benefit<sup>[7]</sup>. Hydroxychloroquine and azithromycin are associated with QT prolongation and caution is advised when considering these drugs in patients with chronic medical conditions (e.g. renal failure, hepatic disease) or who are receiving medications that might interact to cause arrhythmias.

Hydroxychloroquine is currently under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection, and treatment of patients with mild, moderate, and severe COVID-19. In the United States, several clinical trials of hydroxychloroquine for prophylaxis or treatment of SARS-CoV-2 infection are planned or will be enrolling soon. More information on trials can be found at: <https://clinicaltrials.gov/external icon>.

There are no currently available data from Randomized Clinical Trials (RCTs) to inform clinical guidance on the use, dosing, or duration of hydroxychloroquine for prophylaxis or treatment of SARS-CoV-2 infection. Although optimal dosing and duration of hydroxychloroquine for treatment of COVID-19 are unknown, some U.S. clinicians have reported anecdotally different hydroxychloroquine dosing such as: 400mg BID on day one, then daily for 5 days; 400 mg BID on day one, then 200mg BID for 4 days; 600 mg BID on day one, then 400mg daily on days 2-5.

#### Other Drugs

Lopinavir-ritonavir did not show promise for treatment of hospitalized COVID-19 patients with

pneumonia in a recent clinical trial in China<sup>[8]</sup>. This trial was underpowered, and lopinavir-ritonavir is under investigation in a World Health Organization study.

Several other drugs are under investigation in clinical trials or are being considered for clinical trials of prophylaxis or treatment of COVID-19 in the United States and worldwide. Information on registered clinical trials for COVID-19 in the United States is available at: <https://clinicaltrials.gov/external icon>.

#### References

1. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao G. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020 Mar;30(3):269-271.
2. Sheahan TP, Sims AC, Leist SR, Schäfer A, Won J, Brown AJ, Montgomery SA, Hogg A, Babusis D, Clarke MO, Spahn JE, Bauer L, Sellers S, Porter D, Feng JY, Cihlar T, Jordan R, Denison MR, Baric RS. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat Commun*. 2020 Jan 10;11(1):222.
3. Sheahan TP, Sims AC, Graham RL, Menachery VD, Gralinski LE, Case JB, Leist SR, Pirc K, Feng JY, Trantcheva I, Bannister R, Park Y, Babusis D, Clarke MO, Mackman RL, Spahn JE, Palmiotti CA, Siegel D, Ray AS, Cihlar T, Jordan R, Denison MR, Baric RS. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. *Sci Transl Med*. 2017 Jun 28;9(396).
4. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents*. 2020 Mar 4:105932. doi: 10.1016/j.ijantimicag.2020.105932. [Epub ahead of print]
5. Yao X, Ye F, Zhang M, Cui C, Huang B, Niu P, Liu X, Zhao L, Dong E, Song C, Zhan S, Lu R, Li H, Tan W, Liu D. In Vitro Antiviral Activity and Projection of Optimized

Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Clin Infect Dis. 2020 Mar 9. pii: ciaa237. doi: 10.1093/cid/ciaa237. [Epub ahead of print]

6. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends. 2020 Mar 16;14(1):72-73
7. Gautret P, Lagier J, Parola P, Hoang V, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents. In Press.
8. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, Ruan L, Song B, Cai Y, Wei M, Li X, Xia J, Chen N, Xiang J, Yu T, Bai T, Xie X, Zhang L, Li C, Yuan Y, Chen H, Li H, Huang H, Tu S, Gong F, Liu Y, Wei Y, Dong C, Zhou F, Gu X, Xu J, Liu Z, Zhang Y, Li H, Shang L, Wang K, Li K, Zhou X, Dong X, Qu Z, Lu S, Hu X, Ruan S, Luo S, Wu J, Peng L, Cheng F, Pan L, Zou J, Jia C, Wang J, Liu X, Wang S, Wu X, Ge Q, He J, Zhan H, Qiu F, Guo L, Huang C, Jaki T, Hayden FG, Horby PW, Zhang D, Wang C. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med. 2020 Mar 18. doi:

Ref. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html>

### Measures taken to fight against COVID -19 in India

Besides intensive public awareness Indian Govt. has taken some important steps to combat COVID-19 are:

1. Included masks and hand sanitizers under Essential Commodities act vide notification No. S.O. 1087(E) dated 13<sup>th</sup> March 2020.
2. Request of DCGI for quick disposal (3 days) of manufacturing licences for Hand sanitizers vide File No. DCGI/Misc./2020 (96) dated 18.03.2020.
3. Export of surgical masks (2/3ply), ventilators and textile raw materials used in making of masks and coveralls prohibited vide Notification No. 52/2015-2020 dated 19<sup>th</sup> March 2020.
4. Put a Price cap on MRP of masks and hand sanitizers vide notification No. S.O. 1197(E) dated 21<sup>st</sup> March 2020.

### Roche initiates shipment of test kits

Shipments of the first batch of Roche's cobas SARS-CoV-2 Test have begun, with an estimated 400,000 test kits expected to be released this week. The kits will be sent to reference laboratories and a network of hospitals in the US. For details: Seeking Alpha

## Obituary:

**Our sincere homage to the doyen of Pharmacy  
Padmashree Professor Harkishan Singh**



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