Document prepared by Nerve Center of TFORD, Venture Center, Pune

Task Force on Repurposing of Drugs (TFORD) for COVID19

S&T Core Group on COVID19 constituted by PSA to GoI

Molecule Brief: Chloroquine

Ref: TFORD/MB/001	**Date:** 30 Mar 2020
About this document: *This document summarizes information available on drug candidates for COVID19. One Molecule Brief document covers one candidate at a time.*	
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1. Summary Information on Chloroquine

Information About the Candidate for Approved Indication(s)	
Common Name of Drug	Chloroquine
Brand Name	Aralen
Category/ Type	Antimalarial
Drug Bank ID/Link	DB00608 https://www.drugbank.ca/drugs/DB00608
Mode of Action	Chloroquine inhibits the action of heme polymerase in malarial trophozoites, preventing the conversion of heme to hemazoin. Plasmodium species continue to accumulate toxic heme, killing the parasite
Currently Approved for which Indication(s)	Prevention and treatment of Malaria and Amebiasis
Approved Dose	• Prophylaxis Dose - The dosage for prophylaxis is 500 mg (= 300 mg base) administered once per week on exactly the same day of each week. • Treatment Dose- An initial dose of 1 g salt (= 600 mg base) followed by an additional 500 mg (= 300 mg base) after six to eight hours and a single dose of 500 mg (= 300 mg base) on each of two consecutive days. This represents a total dose of 2.5 g chloroquine phosphate or 1.5 g base in three days. 5 mg/kg (8.3 mg/kg of chloroquine phosphate) once weekly on same day each week
Route of Administration	Oral
Safety Profile of drug (dose range in which it has been tested to be safe in humans)	Data not available
Adverse events/Side effects reported at the current approved dose	Headache, loss of appetite, diarrhea, upset stomach, stomach pain, skin rash or itching, hair loss, mood or mental changes
Reported Drug-Drug Interactions	65 major drug interactions 295 moderate drug interactions 15 minor drug interactions
Link to Datasheet	https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/006002s044lbl.pdf

Current TRL level of the Drug	TRL9; Approved Drug
Has the drug been repurposed for any other indication before?	No
Is the Drug being sold in India?	Yes (Generic Versions)
Indian Manufacturer(s)	Merck, IPCA, Ranbaxy, Bayer, Merind, Nicholas, Zota Pharma
International Manufacturer(s)	Sanofi Aventis
Information About the Candidate for COVID-19	
Repurposing Claim	New Indication (COVID-19) + New Dose (not confirmed)
Rationale for Repurposing for COVID19/MoA?	Chloroquine's anti-viral activity is due to its ability to increase endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV. In-vitro data suggests that it can inhibit SARS-CoV-2. • https://www.sciencedirect.com/science/article/pii/S1473309903008065?via%3Dihub • https://www.nature.com/articles/cr2012165#further-reading Illustration of possible MoA: https://science.sciencemag.org/content/367/6485/1412
Proposed use as Primary or Adjuvant?	Primary
Pre-Clinical Data available for COVID-19	Chloroquine effectively inhibits the recently emerged novel coronavirus (SARS-CoV-2) in vitro Chloroquine was found to block COVID-19 infection at low-micromolar concentration, with a half-maximal effective concentration (EC50) of 1.13 μM and a half-cytotoxic concentration (CC50) greater than 100 μM in VeroE6 cells. It functioned at both entry and post entry stages of the SARS-CoV-2 infection in Vero E6 cells. Note – Chloroquine has also found to be effective in inhibiting other SARS and MERS viruses as shown in several in-vitro and in-vivo studies (Ref 3-5 in Reference Section)
Status of Clinical Trials	• Ongoing (See details below) • 1 of the 4 drugs which are being tested in a WHO global multi-centric trial SOLIDARITY ➢ https://www.sciencemag.org/news/2020/03/who-launches-global-megatrial-four-most-promising-coronavirus-treatments ➢ https://science.sciencemag.org/content/367/6485/1412
Number of Trials	7 Ongoing trials Chinese Clinical Trial Registry (ChiCTR2000029939, ChiCTR2000029935, ChiCTR2000029837, ChiCTR2000029826, ChiCTR2000029741, ChiCTR2000029609, ChiCTR2000029542)
Dose being tested for COVID-19	• Day 1-3: 500 mg BID; Day4–10: 250 mg BID 500 mg twice daily for 10 days • Initial dose of 600 mg (of Chloroquine) followed by 300 mg (of chloroquine) 12 hours later on day 1, then 300 mg (of chloroquine) twice daily on days 2-5 https://www.sciencedirect.com/science/article/pii/S0883944120303907?via%3Dihub
Countries where Clinical Trials are being/been done	Netherlands, Belgium, Luxembourg, the United Kingdom, France, and Spain, China https://www.euronews.com/2020/03/23/clinical-trials-starting-in-europe-as-new-drug-offers-hope-of-potential-coronavirus-treatm
Key Data from Clinical Trials	No published data available. A recent publication (Gao et al., 2020), indicates that, "according to the news briefing", "results from more than 100 patients have demonstrated that Chloroquine phosphate is superior to the control

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<tr><td></td><td>treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus negative conversion, and shortening the disease course.
• Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies
•
https://www.sciencedirect.com/science/article/pii/S0166354220301145</td></tr>
<tr><td>TRL Level for COVID19</td><td>TRL > 7 (Ph III/ Ph IV Trials)</td></tr>
<tr><td>IP Status</td><td><table>
<tr><td>Pending applications</td><td>NA</td></tr>
<tr><td>Approved and Active applications</td><td>IN321531
Title: Preparation And Antimalarial Activity Of Novel Quinoline Derivatives,
Assignee: CDRI-CSIR,
Filing date: 31/01/2012
Grant date: 26/09/2019
Expected expiry date: 31/01/2032</td></tr>
<tr><td>Expired or Lapsed application</td><td>467/MUM/2007
Title: Stable Antimalarial Formulations,
Assignee: MCW Healthcare Pvt. Ltd,
Filing date: 12/03/2007
Status: Withdrawn. FER not filed</td></tr>
</table></td></tr>
<tr><td>Other Key References</td><td>1. WHO: Table of Therapeutics
2. https://www.ncbi.nlm.nih.gov/pubmed/15351731
3. https://www.ncbi.nlm.nih.gov/pubmed/27381385
4. https://aac.asm.org/content/53/8/3416</td></tr>
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2. Background information

About TFORD-COVID19

The Principal Scientific Advisor to the GoI, Dr K VijayRaghavan, has constituted a S&T Core Group on COVID19. Under the aegis of the S&T Core Group on COVID19, a Task Force has been constituted focused on Repurposing of Drugs for COVID19 (in short "TFORD-COVID19"). The Task Force is being coordinated by Dr V Premnath, Head, NCL Innovations at CSIR-NCL and Director, Venture Center and Dr Anurag Agarwal, Director, CSIR-IGIB. The Nerve Center for the Coordination is located be at Venture Center, Pune (located in the campus of CSIR-NCL).

Credits

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