**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: Ivermectin

| **Ref:** TFORD/MB/019 | **Date:** 12 April 2020 |
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| ***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 Ivermectin

| **Information About the Candidate for Approved Indication(s)** | |
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| Common Name of Drug | Ivermectin |
| Brand Name | Stromectol |
| Category/ Type | Parasite infections |
| Drug Bank ID/Link | DB00602 (APRD01058)<br>https://www.drugbank.ca/drugs/DB00602 |
| Mode of Action | Ivermectin binds selectively and with high affinity to glutamate-gated chloride ion channels in invertebrate muscle and nerve cells of the microfilaria and activates signaling. This binding causes an increase in the permeability of the cell membrane to chloride ions and results in hyper-polarization of the cell, leading to paralysis and death of the parasite. Ivermectin also is believed to act as an agonist of the neurotransmitter gamma-aminobutyric acid (GABA), thereby disrupting GABA-mediated central nervous system (CNS) neurosynaptic transmission. Ivermectin may also impair normal intrauterine development of *O. volvulus microfilariae* and may inhibit their release from the uteri of gravid female worms. |
| Therapeutic Target | Invertebrate Glycine Receptor Subunit alpha 3 Agonist<br>Invertebrate GABA Receptor Subunit Beta 3 Agonist |
| Is action Host or Virus directed? | Virus |
| Currently Approved for which Indication(s) | 1. For the treatment of intestinal (i.e., nondisseminated) Strongyloidiasis due to the nematode parasite *Strongyloides stercoralis*.<br>2. Treatment of Onchocerciasis (river blindness) due to the nematode parasite *Onchocerca volvulus*.<br>3. Can be used to treat scabies caused by *Sarcoptes scabiei*. |
| Approved Dose | Single oral dose 200 mcg of Ivermectin per kg of body weight |
| Route of Administration | Oral, Topical |
| 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 | Fever, pruritus, and skin rash, joint or muscle pain, painful and tender glands in neck, armpits, or groin, rapid heartbeat |

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| Reported Drug-Drug Interactions | A total of 67 drugs are known to interact with Ivermectin.<br>• 65 moderate drug interactions<br>• 2 minor drug interactions<br>*(Clinicians need to note relevant drug-drug interactions depending on nature of use)* |
| Link to Datasheet | https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/050742s026lbl.pdf |
| Current TRL level of the Drug | Approved |
| Has the drug been repurposed for any other indication before? | No |
| Is the Drug being sold in India? | Yes |
| Indian Manufacturer(s) | Mankind Pharma, Cipla, Genetic Pharma, Zuventus, Micro Vision, Ayntonic Life Sciences, Aurobindo (possible) |
| International Manufacturer(s) | Merck |
| Price of the Drug in India | Rs. 30-70/treatment |
| **Information About the Candidate for COVID-19** | |
| Repurposing Claim | New Indication (COVID-19) + New Dose (not confirmed) |
| Rationale for Repurposing for COVID19/MoA? | 1. Ivermectin shown to have broad anti-viral activity against RNA and DNA virues (HIV, Dengue, West Nile Virus, Influenza, VEEV, Pseudorabies) in-vitro. Its broad spectrum activity is believed to be due to the reliance by many different RNA viruses on IMPα/β1 during infection which it inhibits.<br>2. In-vivo: Ivermectin treatment increases survival of Pserudorabies infected mice.<br>3. Ivermectin was tested in a Phase III trial in Thailand in 2014-2017, against DENV infection, in which a single daily oral dose was observed to be safe and resulted in a significant reduction in serum levels of viral NS1 protein, but no change in viremia or clinical benefit was observed. https://www.sciencedirect.com/science/article/pii/S0166354220302011<br>4. A screening study identified anti-parasitics as a potential class of drugs that show anti-viral activity against SARS-CoV and MERS. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24841273/<br>5. In-vitro evidence shows that Ivermectin is an inhibitor of SARS-CoV-2 infection in cell lines (see below) |
| Proposed use as Primary or Adjuvant? | Primary |
| Pre-Clinical Data available for COVID-19 | 1. The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 *in vitro*<br>Results: with a single addition to Vero-hSLAM cells 2 hours post infection with SARS-CoV-2 clinical isolate from Australia, Ivermectin was able to cause ~5000-fold reduction in viral RNA at 48 h. IC50 was estimated to be 2uM. |
| Status of Clinical Trials | No Ongoing Trials |
| Trial Details | Data not available |
| Key Data from Clinical Trials | Data not available |
| TRL Level for COVID19 | TRL < 5 (Not completed Phase I) |
| IP Status | **Status/ Molecule** — **Ivermectin**<br>Pending applications — 201641033510<br>Title: Pharmaceutical Composition Of Ivermectin And Process For Preparation Thereof<br>Assignee: Aurobindo Pharma Ltd<br>Filing Date: 30/09/2016<br>Publication Date: 06/04/2018<br>Status: Form 3 submitted 07/03/2020<br>IN306571 |

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| | Expired or Lapsed application<br>4529/CHENP/2012<br>Title: A Vermectins And Milbemycins For The Treatment Of Flavivirus Infections<br>Assignee: Consiglio Nazionale Delle Ricerche, Aix-marseille Universite, Katholieke Universiteit Leuven-k.u. Leuven r&d<br>Priority Date: 28/10/2009<br>Publication date: 21/02/2014<br>Status: Abandoned section 21(1) |
| Other Key References | 1.https://www.drugtargetreview.com/news/59414/ivermectin-shows-activity-against-covid-19-in-cell-cultures/ |

## 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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