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: Umifenovir

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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 Umifenovir

Information About the Candidate for Approved Indication(s)	
Common Name of Drug	Umifenovir
Brand Name	Arbidol
Category/ Type	Antiviral
Drug Bank ID/Link	DB13609 https://www.drugbank.ca/drugs/DB13609
Mode of Action	It is a fusion inhibitor. It interacts with the virus hemagglutinin and thus prevents fusion of the viral envelope with cell membranes. It disrupts viral surface protein and prevents virus from entering human host cells.
Therapeutic Target	Multiple in the virus (spike protein, envelope protein etc)
Is action Host or Virus directed?	Virus directed
Currently Approved for which Indication(s)	Influenza, respiratory viral infections in Russia and China
Approved Dose	• For influenza, or other uncomplicated RSV, children 2 – 7, 50 mg; children 7 – 12, 100 mg, and children over 12 and adults, 200 mg, 4 times a day (every 6 hours) for 5 days. • For Severe Acute Respiratory Syndrome (SARS), in children over 12 and adults, 200 mg twice a day for 8 – 10 days. http://www.arbidol.org/dosage.pdf
Route of Administration	Oral
Safety Profile of drug (dose range in which it has been tested to be safe in humans)	200 mg three times daily for 5 days http://www.arbidol.org/normalflu.html#2004efficacy https://www.researchgate.net/journal/1000-503X_Zhongguo_yi_xue_ke_xue_yuan_xue_bao_Acta_Academiae_Medicinae_Sinicae
Adverse events/Side effects reported at the current approved dose	Arbidol is in the category of least toxic drugs (LD50 > 4 g/kg). It has no negative side effects on the human body when taken orally at the recommended dosages.
Reported Drug-Drug Interactions	• No negative side effects have been observed when using this medication in combination with other drugs. • Possible drug interactions between Arbidol and CYP3A4 inhibitors and inducers. https://aac.asm.org/content/57/4/1743

Link to Datasheet	http://www.arbidol.org/dosage.pdf
Current TRL level of the Drug	TRL-9 (Approved Drug)
Has the drug been repurposed for any other indication before?	Broad Spectrum Antiviral activity against respiratory syncytial virus, SARS-CoV, adenovirus, parainfluenza type 5, poliovirus 1, rhinovirus 14, coxsackievirus B5, hantaan virus, Chikungunya virus, HBV and HCV https://www.ncbi.nlm.nih.gov/pubmed/24769245
Is the Drug being sold in India?	Data not available
Indian Manufacturer(s)	Data not available
International Manufacturer(s)	JSC Pharmstandard, Shandong Chuangxin Pharmaceutical Research and Development, Yichang Tianren Pharmaceutical, Shenyang Coupling Biomedical Technology
Price of the Drug in India	Data not available
Information about the candidate for COVID19	
Repurposing Claim	New Indication (COVID 19 treatment and post exposure prophylaxis) + New Dose (not confirmed) http://www.chinaxiv.org/user/download.htm?id=30258
Rationale for Repurposing for COVID19/MoA?	• Has broad spectrum antiviral activity. • Used for SARS treatment. http://dx.doi.org/10.1016/j.antiviral.2014.04.006 • In-vitro evidence for inhibiting SARS virus: Arbidol inhibits SARS-CoV infection of GMK-AH-1 cells at 25, 50 and 100 μg/ml. https://www.ncbi.nlm.nih.gov/pubmed/18756809
Proposed use as Primary or Adjuvant?	Primary
Pre-Clinical Data available for COVID-19	No published data. As per Chinese authorities it was claimed that Arbidol was effective against SARS-CoV-2 at a concentration range of 10-30 μM *in vitro* http://www.sd.chinanews.com/2/2020/0205/70145.html
Status of Clinical Trials	5 Ongoing Phase IV
Trial Details	(See details below)

Trial ID/Link	Type of Trial	Number of patients	Combination/ Dose/Stage of Disease	Primary and Secondary Measures	Has data from the trial been published (Yes/No)
NCT04260594 NCT04252885	Randomized	380	No combination Dose: 2 tablets/time, 3 times/day for 14-20 days Stage: Onset	Primary- Virus negative conversion rate in the first week Secondary- Virus negative conversion rate, Antipyretic rate, Symptom relief time, Finger oxygen improvement rate, disease progression rate, Mortality rate, Incidence of severe adverse reactions, Change curve of peripheral blood lymphocyte count [Time Frame: 14-20 days]	No
NCT04254874	Open, prospective/ retrospective, randomized controlled cohort study	100	Abidol Hydrochloride+ Interferonatomization Dose: 0.2g once, 3 times a day,two weeks Stage: Data	Primary- Rate of disease remission, Time for lung recovery [Time Frame: two weeks] Secondary- Rate of no fever, Rate of respiratory symptom remission, Rate of lung imaging, Rate of CRP,ES,Biochemical criterion (CK,ALT,Mb)recovery , Rate of undetectable viral RNA[Time Frame: two weeks]	No

			not available		
NCT04255017	Open, prospective/ retrospective, randomized controlled cohort study	400	No combination Dose: 0.2g once,3 times a day,2 weeks Stage: Data not available	Rate of disease remission, Time for lung recovery Secondary- Rate of no fever, Rate of respiratory symptom remission, Rate of lung imaging recovery, Rate of CRP,ES,Biochemical criterion(CK,ALT,Mb) recovery, Rate of undetectable viral RNA [Time Frame: two weeks]	No
NCT04273763	Random, open, group sequential design	60	Arbidol, IFNα2b Dose: Data not available Stage: Data not available	Primary- Time to clinical recovery after treatment, Rate of aggravation Secondary- Clinical remission rate, Dynamic changes of oxygenation index, Time to cure, rate to cure, proportion of Clinical recovery, negative COVID-19 nucleic acid results and CT recovery among infected patients, Time to defervescence, Time to cough remission, Time to dyspnea remission, Days of supplemental oxygenation, Rate of patients with requiring supplemental oxygen, Rate of patients with mechanical ventilation, Time of negative COVID-19 nucleic acid results, Rate of negative COVID-19 nucleic acid results, Rate of ICU admission, 28-day mortality	No
ChiCTR2000029592 (Prophylaxis)	Retrospective case-control cohort study	Cohort1- 66 family members Cohort 2- 124 healthcare workers	No combination Dose: 200mg, Tid, 5-10 days Stage: Post exposure prophylaxis	Delay time of PEP after the diagnosis or primary case in family and health care workers cohorts with or without Arbidol	Yes

Key Data from Clinical Trials	A recent publication indicates that Arbidol could reduce the infection risk (Post Exposure Prophylaxis –PEP) of the novel coronavirus in hospital and family settings. Following observations were made– i) 45 family members used Arbidol PEP and 1 became infected ii) 55 health workers used Arbidol PEP and 1 became infected Study: ChiCTR2000029592 http://www.chinaxiv.org/user/download.htm?id=30258
TRL Level for COVID19	TRL-8 (Phase 4)
IP Status	

Status/ Molecule	Umifenovir
Pending applications	Not available
Approved and Active applications	IN310844 Title: Pharmaceutical Dosage Form Comprising One Or More Antiretroviral Active Ingredients Assignee: Evonik Röhm GMBH Priority date: 10/05/2010 Grant date: 04/04/2019 Expected expiry: 03/03/2031
Expired or Lapsed application	547/KOLNP/2010 Title: Antidiabetic Pharmaceutical Composition Assignee: Zakrytoe Aktsionernoe Obschestvo Masterclone Priority date: 14/09/2007

	Publication date: 21/05/2010 Status: Abandoned section 21 (1) IN239640 Title: A Carboxylated Indole Compound Assignee: Shenyang Pharmaceutical University Priority date: 12/03/2004 Grant date: 29/03/2010 Expected expiry: 11/03/2025 Status: Ceased: 11/03/2014
Other Key References	1. https://pubchem.ncbi.nlm.nih.gov/compound/Umifenovir-hydrochloride-monohydrate#section=Information-Sources 2. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.694.3667&rep=rep1&type=pdf 3. http://dx.doi.org/10.1016/j.antiviral.2014.04.006

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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