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: Baloxavir marboxil

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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 Baloxavir marboxil

Information About the Candidate for Approved Indication(s)	
Common Name of Drug	Baloxavir marboxil
Brand Name	Xofluza
Category/ Type	Antiviral (Endonuclease inhibitor)
Drug Bank ID/Link	DB13997 https://www.drugbank.ca/drugs/DB13997
Mode of Action	Baloxavir marboxil is a selective inhibitor of influenza cap-dependent endonuclease which prevents polymerase function and therefore influenza virus mRNA replication. It is a prodrug that is converted by hydrolysis to baloxavir, the active form that exerts anti-influenza virus activity. https://www.ncbi.nlm.nih.gov/pubmed/30288682
Currently Approved for which Indication(s)	Influenza (Japan) Acute Uncomplicated Influenza (US) https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf
Approved Dose	Single dose 20 mg or 40 mg depending on weight https://www.drugbank.ca/drugs/DB13997
Route of Administration	Oral
Safety Profile of drug (dose range in which it has been tested to be safe in humans)	6-80 mg has been tested in Phase I Studies https://www.ncbi.nlm.nih.gov/pubmed/30288682https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210854s001lbl.pdf
Adverse events/Side effects reported at the current approved dose	Adverse events (regardless of causality assessment) reported in at least 1% of adult and adolescent subjects (n=710) who received XOFLUZA at the recommended dose included diarrhea (3%), bronchitis (2%), nausea (1%), nasopharyngitis (1%), and headache (1%). https://www.xofluza.com/hcp/why-xofluza/safety-profile.html
Reported Drug-Drug Interactions	Co-administration with polyvalent cation-containing products may decrease plasma concentrations of baloxavir, which may reduce XOFLUZA efficacy. Avoid co-administration of XOFLUZA with

	dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives or antacids, or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc).
Link to Datasheet	https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210854s001lbl.pdf
Current TRL level of the Drug	TRL 9 ; Approved Drug
Has the drug been repurposed for any other indication before?	No
Is the Drug being sold in India?	No
Indian Manufacturer(s)	CIPLA is reported to be pursuing it https://www.expresspharma.in/latest-updates/csir-iict-ties-up-with-cipla-to-develop-anti-covid-19-drug/
International Manufacturer(s)	Genentech (recently approved - Oct 2019)
Information About the Candidate for COVID-19	
Repurposing Claim	New Indication (COVID-19) + New Dose (not confirmed)
Rationale for Repurposing for COVID19/MoA?	Known anti-viral effect against influenza viruses.
Proposed use as Primary or Adjuvant?	Primary (to be combined with favipiravir or lopinavir/ritonavir)
Pre-Clinical Data available for COVID19	No preclinical data for COVID-19 available https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/ASHP-COVID-19-Evidence-Table.ashx?la=en&hash=B414CC64FD64E1AE8CA47AD753BA744EDF4FFB8C
Status of Clinical Trials	2 Ongoing
Number of Trials	2 Ongoing Trials: CHiCTR2000029548 ChiCTR2000029544
Dose being tested for COVID-19?	80mg on day1, 80mg on day4 and 80mg on day7 as necessary. No more than 3 times administration in total.
Countries where Clinical Trials are being/been done	China
Key Data from Clinical Trials	Data not available
TRL Level for COVID19	TRL > 7 (Ph III/ Ph IV Clinical Trials)
IP Status	**Pending applications**: • IN201747041390 **Title:** Substituted Polycyclic Carbamoylpyridone Derivative **Assignee:** Shionogi & Co., Ltd. **Priority date:** 28/04/2015 **Status:** FER issued **Approved and Active applications**: • IN318238 **Title:** Substituted Polycyclic Carbamoylpyridone Derivative **Assignee:** Shionogi & Co., Ltd. **Priority date:** 24/09/2010 **Grant date:** 14/08/2019 **Expected Expiry:** 21/09/2031 **Expired or Lapsed application**: NA
References	1. https://pubchem.ncbi.nlm.nih.gov/compound/Baloxavir-marboxil 2. https://newdrugapprovals.org/?s=baloxavir&submit= 3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/2

	10854s001lbl.pdf 4. https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf

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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