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**Task Force on Repurposing of Drugs (TFORD) for COVID19**  
 S&T Core Group on COVID19 constituted by PSA to Gol

## Molecule Brief: Favipiravir

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<b>About this document:</b> 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 Favipiravir

<b>Information About the Candidate for Approved Indication(s)</b>	
Common Name of Drug	Favipiravir (Synonyms- Favilavir, Fapilavir)
Brand Name	Avigan in Japan
Category/ Type	Antiviral
Drug Bank ID/Link	DB12466 <a href="https://www.drugbank.ca/drugs/DB12466">https://www.drugbank.ca/drugs/DB12466</a>
Mode of Action	Pyrazinecarbox amide derivative viral RNA polymerase inhibitor. It is a prodrug. Host cell enzymes (cellular kinases) convert Favipiravir into Favipiravir ribofuranosyl phosphate, a form that inhibits virus polymerase without affecting host cellular RNA or DNA synthesis. <a href="https://drugs.ncats.io/drug/EW5GL2X7E0">https://drugs.ncats.io/drug/EW5GL2X7E0</a>
Currently Approved for which Indication(s)	Influenza (Approved in Japan)
Approved Dose	Day 1: 1600 mg twice daily Days 2 through 5: 600 mg twice daily <a href="https://drugs.ncats.io/drug/EW5GL2X7E0">https://drugs.ncats.io/drug/EW5GL2X7E0</a>
Route of Administration	Oral
Safety Profile of drug (dose range in which it has been tested to be safe in humans)	Doses ranging from 30-1600mg was tested in Clinical Studies <a href="https://www.pmda.go.jp/files/000210319.pdf">https://www.pmda.go.jp/files/000210319.pdf</a> <a href="https://www.pmda.go.jp/files/000210319.pdf">https://www.pmda.go.jp/files/000210319.pdf</a>
Adverse events/Side effects reported at the current approved dose	Increase in Uric acid level, Teratogenic
Reported Drug-Drug Interactions	Reported with <a href="#">acetaminophen (inhibitory)</a> and <a href="#">Oseltamivir (synergistic)</a> (Clinicians need to note relevant drug-drug interactions depending on nature of use)
Link to Datasheet	<a href="https://www.pmda.go.jp/files/000210319.pdf">https://www.pmda.go.jp/files/000210319.pdf</a>
Current TRL level of the Drug	TRL 9; Approved Drug
Has the drug been repurposed for any other indication before?	Was given in <a href="#">2014 and 2016 by Japan to West Africa and Guinea respectively to treat Ebola patients. Not much data available</a>

	<a href="#">NCT02329054</a> - Efficacy of Favipiravir Against Ebola (JIKI) <a href="#">NCT02662855</a> - Efficacy of Favipiravir Against Severe Ebola Virus Disease
Is the Drug being sold in India?	Yes
Indian Manufacturer(s)	Glenmark, Strides, Brinton Pharmaceuticals, Cipla (reported to be pursuing it), Lasa Supergenerics (reported to be pursuing it) <a href="https://www.glenmarkpharma.com/sites/default/files/Glenmark-becomes-the-first-pharmaceut-cal-company-in-India-to-receive.pdf">https://www.glenmarkpharma.com/sites/default/files/Glenmark-becomes-the-first-pharmaceut-cal-company-in-India-to-receive.pdf</a> <a href="https://www.expresspharma.in/latest-updates/csir-iict-ties-up-with-cipla-to-develop-anti-covid-19-drug/">https://www.expresspharma.in/latest-updates/csir-iict-ties-up-with-cipla-to-develop-anti-covid-19-drug/</a> <a href="https://health.economicstimes.indiatimes.com/news/pharma/iict-develops-synthetic-process-for-favipiravir-transfers-to-cipla/75490182">https://health.economicstimes.indiatimes.com/news/pharma/iict-develops-synthetic-process-for-favipiravir-transfers-to-cipla/75490182</a> <a href="https://www.expresspharma.in/latest-updates/ict-lasa-succeed-in-favipiravir-drug-synthesis-to-commence-production/">https://www.expresspharma.in/latest-updates/ict-lasa-succeed-in-favipiravir-drug-synthesis-to-commence-production/</a>
International Manufacturer(s)	<a href="#">Fujifilm Toyama Chemical: Japan</a>
<b>Information About the Candidate for COVID-19</b>	
Repurposing Claim	Indication – COVID-19 Dose – See details below
Approval Status	See table below

Country	Approval Type	Date	Stage of Disease	Brand Name/ (Company)	Dose	Reference
Russia	Temporary Approval	1 <sup>st</sup> June 2020	Data not available	Avifavir (Chem Rar Group)	Data not available	<ul style="list-style-type: none"> <li><a href="https://www.trialsite news.com/russia-ministry-of-health-approves-avifavir-favipiravir-for-covid-19-patients-cuts-duration-of-illness-by-over-50/">https://www.trialsite news.com/russia-ministry-of-health-approves-avifavir-favipiravir-for-covid-19-patients-cuts-duration-of-illness-by-over-50/</a></li> </ul>
India	Restricted emergency use	19 <sup>th</sup> June 2020	Mild-Moderate	FabiFlu (Glenmark)	Oral/1800 mg BID /day 1, followed by 800 mg/BID/up to day 14	<ul style="list-style-type: none"> <li><a href="https://www.glenmarkpharma.com/sites/default/files/Glenmark-becomes-the-first-pharmaceut-cal-company-in-India-to-receive.pdf">https://www.glenmarkpharma.com/sites/default/files/Glenmark-becomes-the-first-pharmaceut-cal-company-in-India-to-receive.pdf</a></li> <li><a href="https://cdsco.gov.in/opencms/opencms/system/modules/CDS.CO.WEB/elements/download_file_division.jsp?num_id=NjAwOA==">https://cdsco.gov.in/opencms/opencms/system/modules/CDS.CO.WEB/elements/download_file_division.jsp?num_id=NjAwOA==</a></li> </ul>

Rationale for Repurposing for COVID19/MoA?	Known anti-viral activity. It has been revealed that SARS-CoV-2 has a genome sequence that is 75%–80% identical to that of SARS-CoV and MERS. Since it has been successfully used in SARS-CoV it has been evaluated for its efficacy against SARS-CoV-2.
Proposed use as Primary or Adjuvant?	Primary
Pre-Clinical Data available for COVID19	<ul style="list-style-type: none"> <li>As a prodrug, FPV effectively inhibits SARS-CoV-2 infection in Vero E6 cells (half maximal effective concentration (EC<sub>50</sub>) = 61.88 μmol·L<sup>-1</sup>, half-maximal cytotoxic concentration</li> </ul>

	(CC <sub>50</sub> ) > 400 µmol·L <sup>-1</sup> , selectivity index (SI) > 6.46) <a href="https://www.nature.com/articles/s41422-020-0282-0">https://www.nature.com/articles/s41422-020-0282-0</a> <ul style="list-style-type: none"> <li>Docking study shows Favipiravir binds effectively to SARS-CoV-2 RdRp with a docking score of -6.925 kcal/mol  <a href="https://europepmc.org/article/pmc/pmc7222627">https://europepmc.org/article/pmc/pmc7222627</a></li> </ul>
Status of Clinical Trials	37 Trials (3 in India)
Trial Details	See table below

Trial ID/Link	Type of Trial	No. of patients	Drug Combination/Dose/ Stage of Disease	Primary and Secondary Measures	Has data from the trial been published?
<a href="#">ChiCTR200029548</a>	Randomized, open-label, controlled trial	30	Favipiravir Other Arms: Baloxavir Marboxil, Lopinavir-Ritonavir  Dose: Oral/600 mg/TID; 1600mg first loading dosage for no more than 14 days.  Stage: Data not available	Primary: Time to viral negativity by RT-PCR. Time to clinical improvement: Time from start of study drug to hospital discharge or to NEWS2<2 for 24 hours.	No
<a href="#">ChiCTR200029544</a>	Randomized controlled trial	30	Favipiravir Other Arms: Baloxavir Marboxil,  Dose: Data not available  Stage: Data not available	Primary: Time to viral negativity by RT-PCR. Time to clinical improvement.	No
<a href="#">ChiCTR200029600</a>	Interventional	90	Favipiravir +IFNa Other Arms: IFNa, LPV/R+IFNa  Dose: Data not available  Stage: Within 7 days of disease onset	Primary: Time to viral negativity by RT-PCR. Rate of decrease of virus.	<a href="#">Yes</a>
<a href="#">ChiCTR200030113</a>	Randomized controlled trial	30	Favipiravir  Dose: Data not available  Stage: Virus detected in respiratory or anal swabs after 10 days of standard treatment with roranavir / ritonavir	Primary: Blood routine tests, Liver function examination, Renal function examination, Blood gas analysis, Chest CT examination	No
<a href="#">ChiCTR200030254</a>	Multicenter, randomized, open, positive, parallel-controlled clinical study	240	Favipiravir Other Arms – Arbidol  Dose: Data not available  Stage: Hospitalized	Primary: Clinical recovery rate at Day 7	No ( <a href="#">Preprint available</a> )
<a href="#">NCT04310228</a>	Randomized, Open Label	150	Favipiravir, Favipiravir + Tocilizumab Other Arms – Tocilizumab  Dose: On the 1st day, 1600mg each time, twice a day; from the 2nd to the 7th day, 600mg each	Primary: Clinical cure rate (3 months)	No

			time, twice a day. Oral administration, the maximum number of days taken is not more than 7 days.  Stage: Data not available		
<a href="#">NCT04319900</a>	Randomized, Placebo controlled	150	Favipiravir, Favipiravir + Chloroquine  Dose: On the first day, once for 1600 mg, twice a day; From the 2nd day to the 10th day, once for 600 mg, twice a day; maximum of 10 days for oral administration of the drug.  Stage: Data not available	Primary: Time of Improvement or recovery of respiratory symptoms [ Time Frame: 10 days during the intervention period ] Number of days virus nucleic acid shedding [ Time Frame: 10 days during the intervention period ] Frequency of Improvement or recovery of respiratory symptoms [ Time Frame: 10 days during the intervention period ]	No
<a href="#">CTRI/20/05/025114</a>	Randomized, Open Label, Multicenter	150	Favipiravir  Dose: 3,600 mg (1,800 mg BID) (Day 1) + 1,600 mg (800 mg BID) (Day 2 or later) for up to maximum of 14 days. Mode of Administration: Oral  Stage: Mild to moderate disease	Primary: Time until cessation of oral shedding of SARS-CoV-2 virus [ Time Frame: Up to 28 days ] (Time in days from randomization to a negative SARS-CoV2 RT-PCR result of both oropharyngeal swab and nasopharyngeal swab).for 28 days	No
<a href="#">CTRI/20/06/025799</a>	Randomized, Open Label, Prospective, Comparative, Parallel Group, Multicentre Study	156	Favipiravir  Dose: 1800 mg twice daily on Day 1 and 800 mg twice daily from Day 2 upto maximum 14 days along with supportive care  Stage: Mild to moderate disease	Primary: Time from randomization to negativity in RT-PCR nucleic acid test. [defined as the presence of two consecutive negative results with RT-PCR detection over an interval of 24 hour] for 28 days	No
<a href="#">CTRI/20/06/025957</a>	Randomized Open-Label Study	158	Favipiravir, Favipiravir + Umifenovir  Dose: 3,600 mg (1,800 mg BID) (Day 1) + 1,600 mg (800 mg BID) (Day 2 or later) for up to maximum of 14 days, Mode of Administration: Oral  Stage: Moderate Disease	Primary: Time from randomization to clinical cure (defined as resolution of baseline clinical signs and symptoms of COVID-19 infection and at least 2 point improvement on WHO Ordinal Scale for Clinical Improvement) (Time frame-28 days).	No
<a href="#">NCT04387760</a>	Parallel, prospective, interventional and randomized open label pilot trial	150	Favipiravir Other Arms - Hydroxychloroquine  Dose: 1600mg BID PO day 1, 600mg BID PO day 2 to 10.	Primary: Time to viral clearance (21 days)	No

<a href="#">NCT04376814</a>	Non Randomized, Open Label	40	<p>Stage: Moderate Disease</p> <p>Favipiravir + HCQ Other Arms – lopinavir/R + HCQ</p> <p>Dose: start dose of 1600mg Favipiravir tablets for the first time, and for next time they will be given 600mg of favipiravir tablets three times per day for 7 days</p> <p>Stage: Moderate Disease</p>	Primary: In hospital Mortality (28 days)	No
<a href="#">NCT04402203</a>	Double-blind, placebo-controlled randomized control study	50	<p>Favipiravir</p> <p>Dose: 200 mg tablet will be given orally. Day 1: Tablet Favipiravir 1600 mg twice daily Days 2–Days 10: Tablet 600 mg twice daily.</p>	Primary: Number of participants negative by RT-PCR for the virus at 4-10 days after initiation of therapy. [ Time Frame: at 4 to 10 days of therapy ] Number of participants with lung condition change assessed with X-ray. [ Time Frame: at Day-4, Day-7 and Day-10 of therapy ]	No
<a href="#">NCT04392973</a>	Randomized, open-label, parallel groups	520	<p>Favipiravir + HCQ</p> <p>Dose: 1800 mg (9 tablets) by mouth twice daily for one day, followed by 800mg (4 tablets) twice daily (total days of therapy is 10 days or till hospital discharge)</p> <p>Stage: Moderate to Severe Disease</p>	Primary: Clinical Improvement [ Time Frame: 28 days ]	No
<a href="#">NCT04358549</a>	Open Label, Randomized, Controlled Phase 2	50	<p>Favipiravir</p> <p>Dose: Data not available</p> <p>Stage: Hospitalized</p>	Primary: Time to viral clearance (29 days)	No
<a href="#">NCT04425460</a>	Multi-center, randomized, double-blind, placebo-controlled, phase III clinical study	256	<p>Favipiravir</p> <p>Dose: Day 1 1800 mg x2; Day 2 up to a maximum of 14 days 600 mg x 3</p> <p>Stage: Moderate Disease</p>	Primary: Time from randomization to clinical recovery (28 days)	No
<a href="#">NCT04351295</a>	Open Label	40	<p>Favipiravir</p> <p>Dose: Data not available</p> <p>Stage: Data not available</p>	Primary: Number of patients with viral cure (6 months)	No
<a href="#">NCT04346628</a>	Randomized, Double Blinded, Placebo Controlled Study	120	<p>Favipiravir</p> <p>Dose: 1800 mg on the first dose (day 1) followed by 800 mg twice daily for the next 9 days (days 2-10).</p> <p>Stage: Asymptomatic to Mild Disease</p>	Primary: Time until cessation of oral shedding of SARS-CoV-2 virus [ Time Frame: Up to 28 days ]	No
<a href="#">NCT043</a>	Multi-center,	150	Favipiravir	Primary: Time from	No

<a href="#">36904</a>	randomized, double-blind, placebo-controlled		Dose: Day 1: 1800mg, BID; Day 2 and thereafter: 600mg, TID, for a maximum of 14 days.  Stage: Moderate Disease	randomization to clinical recovery [ Time Frame: 90 days ]	
<a href="#">NCT04359615</a>	Randomized, double-blind, placebo-controlled	40	Favipiravir + HCQ Other Arms – HCQ  Dose: Data not available  Stage: Moderate to Severe Disease	Primary: Time to clinical improvement [ Time Frame: From date of randomization until 14 days later. ]	No
<a href="#">NCT04434248</a>	Adaptive, multicenter, open-label, randomized clinical study	330	Favipiravir  Dose: Data not available  Stage: Moderate to Severe	Primary: Rate of viral elimination by Day 10 [pilot stage, dose selection] [ Time Frame: 10 Days ] Time to viral elimination [pivotal stage] [ Time Frame: 28 Days ] Time to clinical improvement [pivotal stage] [ Time Frame: 28 Days]	No
<a href="#">NCT04373733</a>	Open-label parallel group randomised control trial	450	Favipiravir Other Arms – HCQ + LPV/R+ Azithromycin+Zn	Time to improvement by two points on a seven-category ordinal scale [ Time Frame: Up to 28 days from randomisation ]	No
<a href="#">NCT04411433</a>	Open-label, multicenter, parallel-group, randomized, phase III trial	1000	Favipiravir Favipiravir + Azithromycin Favipiravir + HCQ Other Arms – HCQ + Azithromycin, HCQ  Dose: 3200mg + 1200mg, 3600mg + 1600mg 2x1600 mg (oral) loading dose on day-1 followed by 1200 mg maintenance dose (2x600 mg, 2 times daily) on day-2 to day-5 (5 days in total). 2x1800 mg (oral) loading dose on day-1 followed by 1600 mg maintenance dose (2x800 mg, 2 times daily) on day-2 to day-5 (5 days in total).  Stage: Mild to Moderate Disease	Primary: Time to recovery (discharge) [ Time Frame: 14 days. Decrease in viral load [ Time Frame: 14 days ]	No
<a href="#">NCT04333589</a>	Open Label, Randomized	210	Favipiravir  Dose: On the 1st day, 1600mg each time, twice a day; from the 2nd to the 7th day, 600mg each time, twice a day for not more than 14 days  Stage: Data not available	Primary: Viral nucleic acid test negative conversion rate [ Time Frame: 5 months ]	No
<a href="#">NCT043</a>	Prospective,	320	Favipiravir + LPV/R	Primary: SARS-CoV-2	No

<a href="#">03299</a>	Open label, Randomized, in Multicenter Study		Favipiravir + HCQ+Darunavir/Ritonavir Other Arms - Lopipinavir/ Ritonavir + Oseltamivir, Oseltamivir +Hydroxychloroquine, Lopipinavir/ Ritonavir + Oseltamivir, Darunavir/ Ritonavir + Oseltamivir + Hydroxychloroquine in  Dose: 2400 mg, 2400 mg, and 1200 mg every 8 h on day 1, and a maintenance dose of 1200 mg twice a day  Stage: Mild to Critically Ill	eradication time [ Time Frame: Up to 24 weeks ]	
<a href="#">NCT04345419</a>	Randomized	120	Favipiravir Other Arms – Chloroquine, Nitazoxanide, Ivermectin, Niclosamide, Other drugs  Dose: Data not available  Stage: Data not available	Primary: Number of patients with decreased viral load [ Time Frame: 6 months ]	No
<a href="#">NCT04356495</a> (COVER AGE)	Multi-centre, open-label, randomized controlled superiority multi-arm multi-stage, (MAMS) trial	1057	Favipiravir Other Arms – HCQ, Dietary supplements,  Dose: 12 tablets twice a day the first day (day 0) then 6 tablets twice a day from day 1 to day 9  Stage: Elderly Outpatients With Symptomatic SARS-CoV-2 Infection	Primary: Proportion of participants with an occurrence of hospitalization [ Time Frame: From inclusion (day0) to day 14 ] Death [ Time Frame: From inclusion (day0) to day 14 ]	No
<a href="#">jRCTs041190120</a>	Multicenter, open-label, randomized trial	86	Favipiravir  Dose: Immediate favipiravir arm: Favipiravir administered orally between Day 1 and Day 10, 1800 mg twice a day on Day 1 followed by 800 mg twice a day from Day 2.  Delayed favipiravir arm: Favipiravir administered orally between Day 6 and Day 15, 1800 mg twice a day on Day 6 followed by 800 mg twice a day from Day 7  Stage: Data not available	Primary: Proportion of subjects with clearance of SARS-CoV2 in nasopharyngeal swab by Day 6	No
<a href="#">jRCTs031200026</a>	Multicenter, Single blinded Randomized Controlled, Comparative Study	160	Favipiravir Favipiravir + Nafomastat Mesilate  Dose: Data not available	Primary: Time to alleviation of body temperature, SpO2, and chest image findings, and time to SARS-CoV-2 PCR turn negative	No

<a href="#">IRCTs031190226</a>	Multicenter, Open trial	50	Stage: Data not available Favipiravir  Dose: Data not available  Stage: Data not available	Primary: expected value and 95% CI of ratio of C-reactive protein before versus after the treatment	No
<a href="#">IRCT20200428047228N1</a>	Control group, double-blind, randomized, phase 3	50	Favipiravir + HCQ Other Arms – HCQ Dose: 600 mg of Favipiravir BD on the first day, 600 mg of Favipiravir BD on the second to fifth day  Stage: Hospitalized	Primary: Discharge criteria include: no fever for 3 days, SpO <sub>2</sub> > 93%, relative improvement in CXR - All cause Mortality - Need to Mechanical ventilation -Drug Adverse Effect	
<a href="#">ChiCTR2000030987</a>	Randomized Control Trial	150	Favipiravir + CQ  Dose: Data not available  Stage: course of illness is no more than 14 days	Primary: Improvement or recovery of respiratory symptoms, viral nucleic acid shedding	No
<a href="#">IRCT20151227025726N14</a>	Randomized	84	Favipiravir Other Arms – LPV/R  Dose: dose of 1600 mg BID for one day and then 600 mg BID for totally 7 days  Stage: Hospitalized	Primary: Fever, Cough, Dyspnea	No
<a href="#">IRCT20150808023559N20</a>	Randomized	100	Favipiravir + HCQ Other Arms – LPV/R + HCQ  Dose: Favipiravir tablets (total 1600 mg) followed by Favipiravir 600 mg three times a day for 7 days  Stage: Hospitalized	Primary: Death	No
<a href="#">JAPICCTI-205238</a>	Multicenter, Adaptive, Randomized, Placebo-Controlled, Comparative Study	96	Favipiravir  Dose: Data not available  Stage: Non Severe Pneumonia	Primary: Time to alleviation of body temperature, SpO <sub>2</sub> , and chest image findings, and time to SARS-CoV-2 RT-PCR negativity.	No
<a href="#">CHICTR2000030894</a>	Interventional	150	Favipiravir, Favipiravir + Tocilizumab  Dose: Data not available  Stage: COVID-19 Pneumonia	Primary: Clinical cure rate	No

Key Data from Clinical Trials  
(Note – Only data from interventional trials have been included)

#### Data Published in Journals

- Type of Trial: Open-Label, nonrandomized, Control Study
- Country: China
- Number of patients: 80
- Disease Stage: COVID-19+ve; duration from disease onset to enrolment was less than 7 days
- Interventions: Control - Lopinavir/Ritonavir +IFNa (45); Test - Favipiravir + IFNa (35)



	<ul style="list-style-type: none"> <li>• Dose: Oral/1600mg/BID/D1; 600mg/BID/D2-14</li> <li>• Results: The median time of viral clearance for the patients treated with FPV, was estimated to be 4 d (IQR: 2.5–9), which was significantly shorter than the time for patients in the control group, which was 11 d (IQR: 8–13) (<math>P &lt; 0.001</math>). Two patients in the FPV group turned negative for viral RNA detection in nasopharyngeal swabs at Days 18 and 21, respectively. For patients in the control group, the viral RNA detection all turned negative within 27 d. Chest CT - No significant difference in the improvement rates was found between the two arms on Days 4 and 8 (<math>P &gt; 0.05</math>). However, on Day 14 after treatment, the improvement rates of the chest CT changes in the FPV arm were significantly higher than those in the control arm (91.4% versus 62.2 %, 32/35 versus 28/45, <math>P = 0.004</math>).</li> <li>• Adverse events: The total number of adverse events in the FPV arm of the study was four (11.43%), which was significantly fewer than the 25 adverse events (55.56%) in the control arm (<math>P &lt; 0.001</math>).</li> <li>• Conclusion: Those treated with FPV appeared to have faster viral clearance and better chest imaging change than patients treated with LPV/RTV.</li> <li>•</li> </ul> <p>Reference: <a href="https://www.sciencedirect.com/science/article/pii/S2095809920300631">https://www.sciencedirect.com/science/article/pii/S2095809920300631</a></p>
	<p><b>Data Listed on Trial Registries</b> Data not available</p>
	<p><b>Data from Other Sources ( news articles, pre-prints and unpublished reports)</b></p> <ul style="list-style-type: none"> <li>• Source Type: Pre-Print Article</li> <li>• Type of Trial: Prospective, Multicenter, Open-label, Randomized</li> <li>• Country: China</li> <li>• Number of patients: 240</li> <li>• Disease Stage: COVID-19+ve; hospitalized</li> <li>• Interventions: Control – Umifenovir (120); Test - Favipiravir (120)</li> <li>• Dose: Oral/1600 mg/BID/D1; 600 mg/BID/D2 for 7-10 days</li> <li>• Results: The clinical recovery rate was 51.67% (62/120) in the arbidol group and 61.21%. (71/116) in the favipiravir group after a 7 day's antiviral treatment (<math>P = 0.1396</math>), with the difference of recovery rate between two groups (95% CI) was 0.0954 (-0.0305, 0.2213). For ordinary patients with COVID-19, 7 day's clinical recovery rate was 55.86% (62/111) in the Arbidol group and 71.43% (70/98) in the favipiravir group (<math>P = 0.0199</math>), with the difference of recovery rate between two groups (95% CI) was 0.1557 (0.0271, 0.2843). For critical patients with COVID-19, clinical recovery rate was 0 (0/9) in the arbidol group and 5.56% (1/18) in the favipiravir group (<math>P = 0.4712</math>), with the difference of recovery rate between two groups (95% CI) was 0.0556 (-0.0503, 0.1614); For COVID-19 patients with hypertension and/or diabetes, clinical recovery rate was 51.43% (18/35) in the arbidol group and 54.76% (23/42) in the favipiravir group (<math>P = 0.7704</math>), with the difference of recovery rate between two groups (95% CI) was 0.0333 (-0.1904, 0.2571)</li> <li>• Adverse events: 37 adverse effects cases in the favipiravir group and 28 cases in the arbidol group were observed. The most common adverse events were raised serum uric acid (3 [2.50 %] vs 16 [13.79%], <math>P = 0.0014</math>), more common in patients of the favipiravir group than those in the arbidol group.</li> </ul>

	<ul style="list-style-type: none"> <li>Conclusion: Among patients with COVID-19, Favipiravir, compared to Arbidol, did not significantly improve the clinically recovery rate at Day 7. Favipiravir significantly improved the latency to relief for pyrexia and cough. Adverse effects caused Favipiravir are mild and manageable.</li> <li></li> </ul> <p>Reference: <a href="https://www.medrxiv.org/content/10.1101/2020.03.17.20037432v1.full.pdf">https://www.medrxiv.org/content/10.1101/2020.03.17.20037432v1.full.pdf</a></p> <ul style="list-style-type: none"> <li>Source Type: News Article</li> <li>Type of Trial: Data not available</li> <li>Country: Russia</li> <li>Number of patients: 60</li> <li>Disease Stage: COVID-19+ve; hospitalized; Moderate Disease</li> <li>Interventions: Control – SoC (20); Test - Favipiravir (40)</li> <li>Dose: Data not available</li> <li>Results: These are Interim results from 10 days. According to the results of the 10 days of the clinical trials. Median elimination of the virus took four days compared to nine days with standard therapy, according to the study. Efficacy of the drug is above 80%, a criterion for a drug with high antiviral activity. Following the first four days of treatment, 65% of the 40 patients who took Avifavir tested negative for coronavirus, which is twice as many as in the standard therapy group. By day 10, the number of patients whose tests returned negative results reached 90%. The body temperature of 68% of patients taking Avifavir returned to normal earlier (on the third day) than in the control group (on the sixth day)</li> <li>Adverse events: Avifavir demonstrated safety with no new or previously unreported side effects detected</li> <li>Conclusion: The intermediate data from the Avifavir clinical trials confirms its high efficacy against COVID-19. The final stage of Avifavir clinical trials involving 330 patients in 35 medical centers, approved by the Russian Ministry of Health on May 21, 2020, is ongoing.</li> <li>Reference: <a href="https://rdif.ru/Eng_fullNews/5224/">https://rdif.ru/Eng_fullNews/5224/</a>, <a href="https://economictimes.indiatimes.com/news/international/business/russia-enters-final-stage-of-clinical-trial-of-drug-to-treat-covid-patients/articleshow/75889651.cms">https://economictimes.indiatimes.com/news/international/business/russia-enters-final-stage-of-clinical-trial-of-drug-to-treat-covid-patients/articleshow/75889651.cms</a></li> </ul>
TRL Level for COVID19	TRL- 9 (Approved Drug)
Other Key References	<ol style="list-style-type: none"> <li><a href="https://www.pmda.go.jp/files/000210319.pdf">https://www.pmda.go.jp/files/000210319.pdf</a></li> <li><a href="https://newdrugapprovals.org/tag/favipiravir/">https://newdrugapprovals.org/tag/favipiravir/</a></li> <li><a href="https://pubchem.ncbi.nlm.nih.gov/compound/Favipiravir">https://pubchem.ncbi.nlm.nih.gov/compound/Favipiravir</a></li> <li><a href="https://www.ncbi.nlm.nih.gov/pubmed/28769016">https://www.ncbi.nlm.nih.gov/pubmed/28769016</a></li> <li><a href="#">WHO: Table of Therapeutics</a></li> </ol>

## IP Status:

Pending applications	NA
Approved and Active applications	<p>IN219369 (No WIPO link)  Title: A Pyrazine derivative  Assignee: Toyama Chemical Co. Ltd.  Priority date: 16/02/2000  Grant date: 02/05/2008  Expected expiry date: 14/02/2021</p> <p>IN219547 (No WIPO link)  Title: A Pyrazine derivative  Assignee: Toyama Chemical Co. Ltd.</p>

	<p>Priority date: 16/02/2000 Grant date: 09/05/2008 Expected expiry date: 14/02/2021 <a href="#">IN261641</a> (Divisional IN 219547) Title: Novel pyrazine derivatives or salts thereof, pharmaceutical composition containing the same, and production intermediates thereof Assignee: Toyama Chemical Co. Ltd.</p> <p>Priority date: 16/02/2000 Grant date: 04/07/2014 Expected expiry date: 14/02/2021 <a href="#">IN235048</a> (No link on WIPO site) Title: A novel pyrazine nucleotide or pirazine nucleoside analog Assignee: Toyama Chemical Co. Ltd.</p> <p>Priority date: 14/08/2001 Grant date: 30/06/2009 Expected expiry date: 13/08/2022 <a href="#">IN273554</a> Title: Pharmaceutical composition for treating influenza virus infection Assignee: Toyama Chemical Co. Ltd.</p> <p>Priority date: 16/02/2007 Grant date: 15/06/2016 Expected expiry date: 14/02/2028 <a href="#">IN274639</a> Title: Process for producing an amine salt of 6-fluoro-3-hydroxy-2-pyrazinecarbonitrile Assignee: Toyama Chemical Co. Ltd.</p> <p>Priority date: 27/09/2007 Grant date: 01/09/2016 Expected expiry date: 25/09/2028 <a href="#">IN280086</a> Title: Method for producing dichloropyrazine derivative Assignee: Nippon Soda Co Ltd Priority date: 28/01/2009 Grant date: 09/02/2017 Expected Expiry date: 14/01/2030 <a href="#">IN305027</a> Title: Pyrazino[2,3-D]isoxazole derivative Assignee: Fujifilm Corporation, Toyama Chemical Co., Ltd. Priority date: 12/11/2010 Grant date: 27/12/2018 Expected Expiry date: 11/11/2021</p>
Expired or Lapsed application	<p><a href="#">IN226506</a> (No link on WIPO site) Title: Nitrogen-containing heterocyclic carboxamide derivatives or salts thereof and antiviral agents comprising the same Assignee: Toyama Chemical Co. Ltd. Priority date: 20/08/1998 Grant Date: 19/12/2008 Expired date: Patent has expired on 18/08/2019 <a href="#">4832/KOLNP/2008</a> Title: Anti-foot-and-mouth disease virus agent for animal belonging to family suidae or sheep, and method for prevention or treatment of foot-and-mouth disease in animal belonging to family suidae or sheep Assignee: Toyama Chemical Co. Ltd. Priority date: 31/05/2006 Status: Refused for grant by the controller u/s 3(d) <a href="#">6955/DELNP/2011</a> Title: Tablet and granulated powder containing 6-fluoro-3-hydroxy-2-pyrazinecarboxamide Assignee: Toyama Chemical Co. Ltd. Priority date: 13/03/2009 Status: Refused for grant by the controller u/s 3(d)</p>

## 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**

*Editor: Dr Priya Nagaraj; Contributors: Dr Priya Nagaraj, Dr Vidula Walimbe, Dr Smita Kale, Dr Kirtee Wani, Dr Tejas Shah, Dr Mugdha Lele, Mr Navnath Kadam, Dr Manisha Premnath, Dr Premnath V; Information also contributed by Dr Gopakumar Nair, GNAS and GnanLex.*

### **About Advisory Group**

*The Nerve Center at TFORD-COVID19 has constituted an inter-disciplinary Advisory Group. This Advisory Group reviews the information compiled by the Nerve Center, provides suggestions on data, information sources, organization of data etc. while also providing inputs to refine the analysis and create a structured information base to support decision-making. The Advisory Group also provides expert input and opinions on certain selected points where experience-based inputs are needed. The members of the Advisory Group for each Discussion Paper are listed at <https://nclinnovations.org/covid19/teams/>.*

### **Disclaimer**

*This Molecule Brief is a compilation of information available openly with no opinions or judgments or recommendations. This document is meant to compile high-quality information that can form the basis for informed discussion and decision-making. It is not meant to reflect the Government's position or that of any specific organization or individual. This information should also not be interpreted as guidance for clinical case management.*