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

Molecule Brief: ACEi and ARBs

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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 ACEi and ARBs

(This is a combined sheet for ACEi and ARBs. Lisinopril and Losartan have been used as examples for ACEi and ARB respectively. Evidence in the context of COVID19 and Clinical trial information has been mentioned for both types of drugs)

Information About the Candidate for Approved Indication(s) – Lisinopril (ACEi)	
Common Name of Drug	Lisinopril
Brand Name	Zestril
Category/ Type	Anti-viral, Immuno-modulator
Drug Bank ID/Link	DB00722 (APRD00560) https://www.drugbank.ca/drugs/DB00722
Mode of Action	Lisinopril is an angiotensin converting enzyme inhibitor (ACEi), preventing the conversion of angiotensin I to angiotensin II. This action prevents myocyte hypertrophy and vascular smooth muscle cell proliferation. Lisinopril also inhibits renin's conversion of angiotensin to angiotensin I. https://www.drugbank.ca/drugs/DB00722
Therapeutic Target	Angiotensin-converting enzyme (ACE)
Is action Host or Virus directed?	Host
Currently Approved for which Indication(s)	To treat high blood pressure (Hypertension) in adults and children who are at least 6 years old. Zestril is also used to treat congestive heart failure in adults, or to improve survival after a heart attack. https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019777s064lbl.pdf
Approved Dose	• Hypertension: Initial adult dose is 10 mg once daily. Titrate up to 40 mg daily based on blood pressure response. Initiate patients on diuretics at 5 mg once daily. • Pediatric patients with glomerular filtration rate > 30 mL/min/1.73m2 : Initial dose in patients 6 years of age and older is 0.07 mg per kg (up to 5 mg total) once daily. • Heart Failure: Initiate with 5 mg once daily. Increase dose as tolerated to 40 mg daily. • Acute Myocardial Infarction (MI): Give 5 mg within 24 hours of MI.

	followed by 5 mg after 24 hours, then 10 mg once daily. • Renal Impairment: For patients with creatinine clearance ≥ 10 mL/min and ≤ 30 mL/min, halve usual initial dose. For patients with creatinine clearance < 10 mL/min or on hemodialysis, the recommended initial dose is 2.5 mg
Route of Administration	Oral
Safety Profile of drug (dose range in which it has been tested to be safe in humans)	Up to 40mg https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019777s064lbl.pdf
Adverse events/Side effects reported at the current approved dose	Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019777s064lbl.pdf
Reported Drug-Drug Interactions	• Diuretics: Excessive drop in blood pressure. • NSAIDS: Increased risk of renal impairment and loss of antihypertensive efficacy • Dual inhibition of the renin-angiotensin system: Increased risk of renal impairment, hypotension and hyperkalemia • Lithium: Symptoms of lithium toxicity • Gold: Nitritoid reactions have been reported https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019777s064lbl.pdf *(Clinicians need to note relevant drug-drug interactions depending on nature of use)*
Link to Datasheet	https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019777s064lbl.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?	Yes
Indian Manufacturer(s)	Cipla, GSK, Aventis
International Manufacturer(s)	G.L. Pharma, Austria, Rafarm, Greece, Sandoz, Malaysia, Hexal, Germany
Cost of the Drug in India	150 – 200 INR per strip of 15 tablets

Information About the Candidate for Approved Indication(s) – Losartan (ARB)	
Common Name of Drug	Losartan
Brand Name	COZAAR® (Losartan potassium) tablets
Category/ Type	Anti-viral/Immuno-modulatory
Drug Bank ID/Link	DB00678 (APRD00052) https://www.drugbank.ca/drugs/DB00678
Mode of Action	Losartan is an Angiotensin II Receptor Blocker (ARB). It reversibly and competitively prevents angiotensin II binding to the AT_1 receptor in tissues like vascular smooth muscle and the adrenal gland. Losartan and its active metabolite bind the AT_1 receptor with 1000 times more affinity than they bind to the AT_2 receptor. The active metabolite of losartan is 10-40 times more potent by weight than unmetabolized losartan as an inhibitor of AT_1 and is a non-competitive inhibitor. Losartan's prevention of angiotensin II

	binding causes vascular smooth muscle relaxation, lowering blood pressure. Angiotensin II would otherwise bind to the AT_1 receptor and induce vasoconstriction, raising blood pressure https://www.drugbank.ca/drugs/DB00678
Therapeutic Target	Type-1 Angiotensin II Receptor antagonist
Is action Host or Virus directed?	Host
Currently Approved for which Indication(s)	• Treatment of hypertension, to lower blood pressure in adults and children greater than 6 years old. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. • Reduction of the risk of stroke in patients with hypertension and left ventricular hypertrophy. • Treatment of diabetic nephropathy with an elevated serum creatinine and proteinuria in patients with type 2 diabetes and a history of hypertension.
Approved Dose	Hypertension: • Usual adult dose: 50 mg once daily. • Usual pediatric starting dose: 0.7 mg per kg once daily (up to 50 mg). Hypertensive Patients with Left Ventricular Hypertrophy: • Usual starting dose: 50 mg once daily. Nephropathy in Type 2 Diabetic Patients: • Usual dose: 50 mg once daily. • Increase dose to 100 mg once daily if further blood pressure response is needed.
Route of Administration	Oral
Safety Profile of drug (dose range in which it has been tested to be safe in humans)	Up to 100mg https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020386s058lbl.pdf
Adverse events/Side effects reported at the current approved dose	Dizziness, Upper Respiratory Infection, Nasal Congestion, And Back Pain
Reported Drug-Drug Interactions	• Agents increasing serum potassium: Risk of hyperkalemia. • Lithium: Risk of lithium toxicity. • NSAIDs: Increased risk of renal impairment and reduced diuretic, natriuretic, and antihypertensive effects. • Dual inhibition of the renin-angiotensin system: Increased risk of renal impairment, hypotension, syncope, and hyperkalemia. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020386s058lbl.pdf
Link to Datasheet	https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020386s058lbl.pdf https://www.merck.com/product/usa/pi_circulars/c/cozaar/cozaar_pi.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?	Yes
Indian Manufacturer(s)	IPCA, INTAS, Wockhardt, Torrent, FDC, Cipla

International Manufacturer(s)	Getz Pharma, Philippines, GeoLab, Brazil., Biosintética, Brazil., Mylan, Spain., Daiichi Sankyo Espha, Japan., Pfizer Japan, Japan., Centrafarm, Netherlands. etc.
Cost of the Drug in India	15 – 25 INR per strip of 15 tablets

Information About the Candidates for COVID-19 – For ACEi and ARBs	
Repurposing Claim	New Indication (COVID-19) + New Dose (not confirmed)
Rationale for Repurposing for COVID19/MoA?	SARS-CoV-2 uses the ACE2 receptor to enter human host cells. ACE2 has a broad expression pattern with strong expression noted in the gastrointestinal system, heart, and kidney and lungs (type 2 alveolar cells) and breaks down Angiotensin II. https://www.nature.com/articles/s41586-020-2012-7 https://jamanetwork.com/journals/jama/fullarticle/2763803 Rationale for Hypothetical Benefit: In-vivo studies (not in COVID-19 context) suggest that expression of ACE2 is can increase with administration of ACEi/ARBs. In-vivo lung injury mouse models shows ACE2 can reduce inflammation, which might be beneficial in COVID-19. https://pubmed.ncbi.nlm.nih.gov/28935640/ https://pubmed.ncbi.nlm.nih.gov/31393582/ https://pubmed.ncbi.nlm.nih.gov/31645418/ https://www.nejm.org/doi/full/10.1056/NEJMsr2005760 Rationale for Hypothetical Harm: In-vivo studies (not in COVID-19 context) suggest that expression of ACE2 is can increase with administration of ACEi/ARBs. This could mean allowing for more SARS-CoV-2 binding. Virus binding to ACE2 might also prevent ACE2 from performing its function of breaking down Angiotensin II. In the context of COVID-19, this could mean increasing patient susceptibility to viral host cell entry and propagation. However, role of ACE2 expression on COVID-19 pathogenesis and mortality is not well understood. https://www.ahajournals.org/doi/full/10.1161/circulationaha.104.510461 https://www.ahajournals.org/doi/10.1161/01.HYP.0000124667.34652.1a https://jamanetwork.com/journals/jama/fullarticle/2763803 https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600(20)30116-8.pdf Various Clinical Management Guidelines (NIH, AHA) have recommended continued use of ACEi/ARB for COVID-19 patients who are already on these medications. https://www.covid19treatmentguidelines.nih.gov/ https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19 https://www.covid19treatmentguidelines.nih.gov/concomitant-medications/ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7121452/
Proposed use as Primary or Adjuvant?	Primary
Pre-Clinical Data available for COVID-19	Data not available
Status of Clinical Trials	19 ongoing trials for ACEi and ARBs – 17 Interventional + 2 Observational – Trials with ACEi and ARBs other than Lisinopril and Losartan have been included.
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?
NCT04351581	Randomized	215	ACEi/ ARB in combination or alone. Arms – Experimental continuation, Experimental Discontinuation ACEi: Benazepril/ Captopril/ Enalapril/ Fosinopril/ Lisinopril/ Perindopril/ Quinapril/ Ramipril/ Trandolapril. ARBs: Candesartan/ Eprosartan/ Irbesartan/ Losartan/ Olmesartan/ Telmisartan/ Valsartan Dose: Data not available Stage: Data not available	Primary: Days alive and out of hospital within 14 days after recruitment. Secondary: Severe respiratory insufficiency, Referral to treatment in an intensive care unit, Death	No
NCT04330300	Randomized, Open Label	2414	ACE Inhibitor – Control Arm (Benazepril, captopril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, trandolapril) ARB – Hypertensive Arm (Candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan) Other Arms – Thiazide or Thiazide-like diuretics, Calcium Channel Blockers Dose: Data not available Stage: Data not available	Primary: Number of Covid-19 positive participants who die, require intubation in ICU, or require hospitalization for non-invasive ventilation (NIV) [Time Frame: 12 months]. Secondary: Time from randomization to the first occurrence of any of the clinical events above. Number of Covid-19 positive participants who die [Time Frame: 12 months] Number of Covid-19 positive participants who require intubation in intensive care unit (ICU) [Time Frame: 12 months] Number of Covid-19 positive participants who require hospitalization for non-invasive ventilation (NIV) [Time Frame: 12 months] Number of SARS-CoV-2 positive participants [Time Frame: 12 months] Maximum troponin T value (ng/L) among Covid-19 positive participants who require acute hospitalization [Time Frame: 12 months] 24 hour mean systolic BP	No

				(mmHg) on ambulatory BP monitoring [Time Frame: 12 months] All-cause mortality [Time Frame: 12 months]	
NCT04318418 (Observational)	Observational Retrospective	5000	ACE ior ARBs (Drugs not specified) Dose: Data not available Stage: Patients who developed severe COVID-19 disease	Primary: Severe COVID-19 [Time Frame: 1 month] Severity pneumonia or acute respiratory distress syndrome by COVID-19. Secondary Death [Time Frame: 1 month] Death by COVID-19	No
NCT04345406	Interventional Randomized	60	ACEIs + Chloroquine (Conventional treatment) Drug: ACEIs Captopril or enalapril Other Name: Enalapril, Captopril Dose: Data not available Stage: Data not available	Primary: Number of patients with virological cure [Time Frame: 6 months] number of patients with virological cure	No
NCT04367883 (Observational)	Observational	2574	ACEi and ARBs (Drugs not specified) Dose: Data not available Stage: Data not available	Primary: Hospital output [Time Frame: from March 1, 2020.] exitus vs hospital output and length of the hospital stay. Secondary: Length of ICU admission [Time Frame: From March 1, 2020.]	No
NCT04335786	Interventional, Randomized	651	ARB: Valsartan Dose: dosage and frequency titrated to blood pressure with 80mg or 160mg tablets up to a maximum dose of 160mg b.i.d Stage: Data not available	Primary: First occurrence of intensive care unit admission, mechanical ventilation or death [Time Frame: within 14 days] Secondary: Death [Time Frame: Within 14 days, 30 days, 90 days and at 1 year] Mechanical ventilation [Time Frame: within 14 days] ntensive care unit admission [Time Frame: within 14 days] Occurrence of acute kidney injury [Time Frame: Within 14 days]	No
NCT04355936	Interventional, Randomized	400	ARBs: Telmisartan Dose: 80 mg Telmisartan twice daily plus SOC	Primary: C reactive protein [Time Frame: Days 1, 8 and 15 after enrollment] Secondary: Number of opacified quadrants on	No

			Stage: Data not available	lung Rx [Time Frame: Days 1, 8 and 15 after enrollment] [Time Frame: Within 15 days] Intensive care unit admission [Time Frame: Within 15 days] Death [Time Frame: Within 15 days, 30 days, 90 days] LDH [Time Frame: Days 1, 8 and 15 after enrollment] Troponin Time to mechanical ventilation [Time Frame: Within 15 days]	
NCT04360551	Interventional, Randomized	40	ARB: Telmisartan Dose: 40 mg po daily x 21 days. Stage: Data not available	Primary: Maximum clinical severity of disease [Time Frame: Over the 21 day period of study] Secondary: Incidence of treatment emergent adverse events [Time Frame: Through study completion at day 21 of study] Renin angiotensin system peptides [Time Frame: At each study time point (day 4, day 10, day 21)] Plasma biomarkers [Time Frame: At each study time point (day 4, day 10, day 21)	No
NCT04359953	Interventional, Randomized	1600	ARB: Telmisartan Other Arms – HCQ , Azithromycin Dose: 40mg of Telmisartan twice a day during 14 days Stage: Data not available	Primary: Two-weeks survival rate [Time Frame: Day 14] Secondary: 27 measures – See trial link for details	No
NCT04356495	Interventional, Randomized	1057	ARB: Telmisartan Other Arms – Favipiravir Dose: Telmisartan (Micardis® 20 mg) during 10 days Stage: Data not available	Primary: Proportion of participants with an occurrence of hospitalization [Time Frame: From inclusion Day 0 to day 14] Death [Time Frame: From inclusion (day0) to day 14] Secondary: 13 measures – See trial link for details	No
NCT04394117	Interventional, Randomized	605	ARBs + SOC Drugs – Candesartan/ Eprosartan/Irbesartan/ Losartan/Olmesartan/ Telmisartan/Valsartan	Primary: 7-Point National Institute of Health Clinical Health Score [Time Frame: 28 Days]	No

EudraCT 2020-001435-27	Multiarm, multi-stage (MAMS) randomized	1057	ARB: Telmisartan Other Arms – HCQ, Imatinib, Favipiravir Dose: 20mg Telmisartan Stage: Data not available	Primary: Proportion of participants with an occurrence of hospitalization and/or death between D0 and D14 in each arm.	No
EudraCT 2020-001303-16	Randomized, Multi-Centre	Data not available	ARBs: Telmisartan Dose: 80 mg Stage: Data not available	Primary: 2 week survival rate Secondary: 24 measures. See trial link for details	No
NCT04312009	Interventional, Randomised	200	ARB: Losartan Drug: Losartan; 50 mg daily; oral administration Stage: Data not available	Primary: Difference in Estimated (PEEP adjusted) P/F Ratio at 7 days [Time Frame: 7 days] Secondary: 21 measures. See trial link for details	No
NCT04311177	Interventional, Randomised	580	ARBs: Losartan Dose: 25 mg daily; oral Stage: Data not available	Primary: Hospital Admission [Time Frame: 15 days] Secondary: 13 measures. See trial link for details	No
NCT04328012	Interventional, Randomised	4000	ARBs: Losartan Other Arms – HCQ, Lopinavir/Ritonavir Dose: 25 mg po QD X 5-14 days depending on availability Stage: Data not available	Primary: National Institute of Allergy and Infectious Diseases COVID-19 Ordinal Severity Scale (NCOSS) [Time Frame: 60 days] Secondary: Hospital length of stay (LOS) [Time Frame: 60 days] Intensive care unit level LOS [Time Frame: 60 days] Mechanical ventilation [Time Frame: 60 days] difference in length of use of mechanical ventilation between the four treatment groups. Survival [Time Frame: 60 days]	No
NCT04335123	Interventional, Single Group Assignment	50	ARBs: Losartan Dose: Losartan 25 mg QD from day 0 to day 3. Dose escalation to 50 mg QD until study completion Stage: Patients with COVID-19 and respiratory failure	Primary: Number of participants with treatment-related adverse events as assessed by protocol definition of AE [Time Frame: 14 days of losartan treatment] Secondary: Number of days on supplemental oxygen in respiratory failure due to COVID-19 [Time Frame: 14 days of	No

				losartan treatment] Incidence of transfer to ICU from non-ICU hospital bed [Time Frame: 14 days of losartan treatment] ICU length of stay (days) [Time Frame: 14 days of losartan treatment] I30-day mortality rate [Time Frame: 30 days after diagnosis of COVID-19] Hospital length of stay (days) [Time Frame: 14 days of losartan treatment] Cumulative incidence of severe adverse events [Time Frame: 14 days of losartan treatment] Cumulative incidence of adverse events [Time Frame: 14 days of losartan treatment] Change from baseline in oxygenation [Time Frame: 14 days of losartan treatment] Incidence (and length in days) of extracorporeal membrane oxygenation use [Time Frame: 14 days of losartan treatment] Incidence (and length in days) of renal replacement therapy use [Time Frame: 14 days of losartan treatment] Intolerance of high dose (50mg) losartan after tolerating 25mg [Time Frame: 14 days of losartan treatment] Intolerance of high dose (50mg) losartan after tolerating 25mg	
NCT04343001	Interventional, Randomised	10000	ARBs: Losartan Losartan + Asprin Losartan + Simvastatin Losartan + Simvastatin + Asprin Other Arms – Simvastatin, Asprin, Dose: 100mg once daily Losartan Stage: Data not available	Primary: Death [Time Frame: up to 28 days of randomisation] Secondary Myocardial infarction [Time Frame: up to 28 days of randomisation] Congestive cardiac failure [Time Frame: up to 28 days of randomisation] Severe cardiac arrythmia [Time Frame: up to 28 days of randomisation] Myocarditis [Time Frame: up to 28 days of randomisation] Respiratory failure including ARDS	No

				[Time Frame: up to 28 days of randomisation] Viral pneumonitis [Time Frame: up to 28 days of randomisation] Acute renal failure [Time Frame: up to 28 days of randomisation] Sepsis [Time Frame: up to 28 days of randomisation] Stroke [Time Frame: up to 28 days of randomisation] Gastrointestinal bleeding [Time Frame: up to 28 days of randomisation] Receipt of non invasive or mechanical ventilation [Time Frame: up to 28 days of randomisation] Ability to self care at hospital discharge [Time Frame: up to 28 days of randomisation]	
NCT04340557	Interventional, Randomised	200	ARB: Losartan + SOC Dose: 12.5mg (investigator has option to increase dose on days 2-10 based on tolerance of SBP) of losartan taken twice daily for up to 10 days. Stage: Data not available	Primary: Mechanical ventilation [Time Frame: from date of patient admission to date of patient discharge or date of death, whichever came first, assessed up to 45 days] Secondary: ICU transfer [Time Frame: from date of patient admission to date of patient discharge or date of death, whichever came first, assessed up to 45 days] Oxygen therapy [Time Frame: from date of patient admission to date of patient discharge or date of death, whichever came first, assessed up to 45 days]	No

Key Data from Clinical Trials	No published data from Clinical Trials WHO has reported a rapid review study where data from 11 observational studies (8 – China, 3- Italy, USA, UK) was reviewed. Conclusion**:** No studies were found that were designed to directly assess whether ACEi/ARBs increase the risk of acquiring COVID-19. After adjustment for confounders, history of ACE inhibitor or ARB use was not found to be associated with increased severity of COVID-19 illness. https://www.who.int/news-room/commentaries/detail/covid-19-and-the-use-of-angiotensin-converting-enzyme-inhibitors-and-receptor-blockers Other Observational Studies: • Study: Data for over 12,500 tested for COVID-19 in New York Result: No substantially higher risk (by ≥10 percentage points) of severe Covid-19 associated with use of ACE Inhibitors. A substantial difference (≥10 percentage points) in the likelihood of severe illness was ruled out with at least 97.5% certainty with the use of ACE Inhibitors. https://www.nejm.org/doi/full/10.1056/NEJMoa2008975

	• Study: Data from 6272 COVID-19 confirmed patients in Italy. Result: In a conditional logistic-regression multivariate analysis, ACE inhibitors were not associated with the likelihood of SARS-CoV-2 infection. An additional analysis comparing patients with severe or fatal infections with matched controls also did not show an association between these drugs and severe Covid-19. https://www.nejm.org/doi/full/10.1056/NEJMoa2006923
TRL Level for COVID19	TRL>7; (Phase III/IVTrials)
Other Key References	None

IP Status

Status/ Molecule	Lisinopril
Pending applications	Not applicable
Approved and Active applications	276937 Title: A process for the preparation of 6-(5-chloropyrid-2-yl)-5-(4-methylpiperazin-1-yl)-carbonyloxy-7-0x0-5,6-dihydropyrrolo-[3,4-b]-pyrazine and it's enantiomerically enriched isomer Assignee: Mylan Laboratories Limited Priority date: 27/04/2007 Grant date: 07/11/2016 Expected expiry date: 27/04/2027
Expired or Lapsed application or examination request not filed	706/CHE/2003 Title: An improved process for the preparation of Lisinopril useful as angiotensin-converting enzyme inhibitors a novel intermediate for the preparation of Lisinopril and a process for its preparation Assignee: M/S. Neuland laboratories limited Filing date: 05/09/2003 Publication date: 14/09/2007 Status: No updates on Indian patent site 870/MUM/2008 Title: An improved process for purification of L-Proling, N2-[(1s)-1-ethoxyearbonyl-3-phenylpropy1]-N6-(Trifuoroacetyl)-L-Lysyl Assignee: Calyx chemicals and pharmaceuticals Ltd Filing date: 17/04/2008 Publication date: 30/10/2009 Status: Abandoned under section U/S 21(1) 2504/MUM/2008 Title: A novel process for desalination of Lisinopril Assignee: Calyx Chemicals And Pharmaceuticals Ltd Filing date: 01/12/2008 Publication date: 13/08/2010 Status: Abandoned under section U/S 21(1) 201711020236 Title: Formulation and evaluation of controlled drug delivery of Lisinopril Assignee: Devgun Manish, Grover Ish, Singh Balvinder Filing date: 09/06/2017 Publication date: 01/09/2017 Status: Abandoned under section U/S 21(1)

Status/ Molecule	Losartan
Pending applications	201711023545 Title: A neuroprotective agent comprising ester of Losartan carboxylic acid and ascorbic acid Assignee: Chairman, Defence Research & Development Organization, Siksha Anusandhan University, Bhubaneswar Filing Date: 04/07/2017 Publication date: 11/01/2019 Status: Pending 201941000177

	Title: Design and development of floating tablets of Losartan potassium Inventors: Bodepudi Srikanth, Varra Madhu Sudharsan Filing Date: 02/01/2019 Publication date: 11/01/2019 Status: Pending. Deadline to file request for examination is 02/01/2023
Approved and Active applications	237665 Title: An improved and practical process for the preparation of Losartan Assignee: Suven Life Sciences Ltd Filing Date: 31/08/2005 Grant date: 08/01/2010 Expected expiry date: 31/08/2025 301193 Title: An improved process for preparing Losartan potassium Patentee: Alembic Pharmaceuticals Ltd Filing Date: 18/05/2011 Grant date: 19/09/2018 Expected expiry date: 18/05/2031
Expired or Lapsed application or examination request not filed	979/KOL/2005 Title: Pharmaceutical formulation of Losartan Assignee: Lupin Limited Priority Date: 27/10/2005 Publication date: 06/07/2007 Status: Application has been refused under section 15 226992 (No link on WIPO site) Title: Crystalline or crystallized ACD addition salt of Losartan and purification method of Losartan Assignee: Sumitomo Chemical Company Limited Priority Date: 06/12/1999 Grant date: 31/12/2008 Status: Patent Expired 02/12/2013 193625 Title: Process for the crystallization of Losartan potassium Patentee: Aurobindo Pharma Ltd Filing Date: 18/05/2001 Grant date: 06/12/2005 Status: Patent ceased on 16/03/2006 219489 Title: A process for preparing amorphous Losartan potassium Patentee: Teva Pharmaceutical Industries, Ltd. Priority Date: 14/11/2001 Grant date: 07/05/2008 Status: Patent ceased on 15/11/2010 2112/DELNP/2008 (Divisional to: 1286/DELNP/2004) Title: Losartan potassium in a crystalline form Patent Applicant: Teva Pharmaceutical Industries Ltd. Priority Date: 14/11/2001 Publication date: 18/04/2008 Status: Abandoned 2712/DELNP/2008 (Divisional to Application Number: 1286/DELNP/2004) Title: Amorphous Losartan potassium Patent Applicant: Teva Pharmaceutical Industries Ltd. Priority Date: 14/11/2001 Publication date: 25/07/2008 Status: Abandoned 568/MAS/2002 Title: Novel crystalline form-III of 2-buty l-4-chloro-1-[[2'-(1h-tetrazol-5-y1)[1,1'-biphenyl]-4-yl]methyl]-1h-imidazole-5-methanol potassium salt (Losartan potassium) Assignee: Dr. Reddy's laboratories Filing Date: 29/07/2002 Publication date: 27/07/2007 Status: No updates on Indian patent site 1095/DEL/2002 Title: Process for the preparation of novel amorphous form of Losartan potassium Assignee: Ranbaxy Laboratories Limited Filing Date: 31/10/2002 Publication date: 28/01/2005 Status: Abandoned

	72/CHE/2003 Title: Novel amorphous form of 2-n-butyl-4-chloro-5-hydroxymethyl-1-[[2'-(1h-tetrazol-5-yl)biphenyl-4-yl]imidazole potassium salt Assignee: Dr. Reddy's Laboratories Ltd Filing date: 28/01/2003 Publication date: 27/07/2007 Status: No updates on Indian patent site 194056 Title: Process for preparation of amorphous form of Losartan potassium Assignee: Hetero Drugs Limited Filing Date: 25/02/2003 Grant date: 19/12/2005 Status: Patent ceased on 25/02/2011 202/DEL/2003 Title: Crystalline forms of Losartan potassium and process for production thereof Assignee: Ranbaxy Laboratories Limited Filing Date: 28/02/2003 Publication date: 12/02/2010 Status: Application abandoned 208/CHE/2003 Title: Novel crystalline form-iv of 2-n-butyl-4-chloro-5-hydroxymethyl-1-[[2!-(1h-tetrazol-5yl)-biphenyl-4-yl] methyl]imidazole potassium (losartan potassium) and process for the preparation thereof Assignee: Dr. Reddy's laboratories ltd Filing date: 13/03/2003 Publication date: 06/07/2007 Status: No updates on Indian patent site 196095 Title: An improved process for the synthesis of an Angiotensin II receptor antagonist Patentee: IPCA Laboratories Ltd. Filing Date: 03/04/2003 Grant date: 19/09/2005 Status: Patent ceased on 03/04/2008 234979 Title: Process for the preparation of trityl Losartan potassium form I Assignee: Cadila Pharmaceuticals Ltd. Filing Date: 04/09/2003 Grant date: 23/06/2009 Status: Patent ceased on 06/09/2010 211352 Title: Improved process for the manufacture of Losartan potassium Assignee: IPCA Laboratories Limited Filing Date: 06/01/2004 Grant date: 26/10/2007 Status: Patent ceased on 06/01/2011 3688/DELNP/2005 Title: Co-precipitated amorphous Losartan and dosage forms comprising the same Assignee: Ranbaxy Laboratories Limited Priority Date: 21/01/2004 Publication date: 07/12/2007 Status: Application abandoned under the section 21(1) 502/CHE/2004 (No link on WIPO site) Title: Amorphous Form Of Losartan Potassium Patent Applicant: Hetero Drugs Limited Filing Date: 02/06/2004 Publication date: 06/06/2006 Legal Status: No updates on Indian patent site 210131 Title: A process for preparation of 2-n-butyl-4-chloro-1-{[2'-(2-triphenylmethyl-2h-tetrazole-5-yl)-1-1'-biphenyl-4-yl]methyl}-1h- imidazole -5-methanol (intermediate of Losartan) Patentee: Matrix Laboratories Ltd Filing Date: 06/10/2004 Grant date: 21/09/2007 Status: Patent ceased on 25/12/2007 1383/MUM/2004 (No link on WIPO site) Title: Amorphous Losartan potassium and process for its preparation Assignee: Lupin Limited

	Filing date: 21/12/2004 Publication date: 21/07/2006 Status: Application has been abandoned under section 21(1) 3818/CHENP/2007 Title: Method for the production of Losartan Assignee: Ratiopharm Ghbh Priority date: 03/02/2005 Publication date: 21/12/2007 Status: Application abandoned 6761/DELNP/2007 Title: Oral pharmaceutical form of Losartan Assignee: Flamel Technologies Filing date: 31/08/2007 Priority date: 21/02/2005 Publication date: 21/09/2007 Status: Application abandoned 238064 Title: an improved process for the preparation of Losartan Assignee: Suven Life Sciences Limited Filing date: 16/08/2005 Grant date: 20/01/2010 Status: Patent ceased on 20/04/2010 598/MUM/2006 (No link on WIPO site) Title: An improved process for the manufacture of Losartan potassium Assignee: Unichem Laboratories Limited Filing date: 17/04/2006 Publication date: 21/11/2008 Status: No updates on Indian patent site 1390/MUM/2006 Title: Pharmaceutical composition comprising Losartan or salts thereof and method of preparing the same Assignee: Wockhardt Limited Filing date: 31/08/2006 Publication date: 25/07/2008 Status: No updates on Indian patent site 259226 Title: An improved process for preparation of Losartan potassium in crystalline form-1 Assignee: Cadila Healthcare Limited Filing Date: 25/01/2007 Grant date: 04/03/2014 Status: Patent ceased on 25/01/2018 827/MUM/2007 Title: Pharmaceutical composition comprising Losartan or salts thereof Assignee: Wockhardt Ltd Filing Date: 27/04/2007 Publication date: 22/05/2009 Status: No updates on Indian patent site 924/DEL/2007 Title: Aloe vera oil: a new skin permeation enhancer Assignee: Jamia Hamdard University Filing Date: 27/04/2007 Publication date: 16/01/2009 Status: Application abandoned 972/CHE/2007 Title: Crystalline form of Losartan potassium Assignee: Matrix Laboratories Ltd Filing date: 08/05/2007 Publication date: 28/11/2008 Status: No updates on Indian patent site 960/MUM/2007 Title: Improved and environment friendly preparation process for Losartan potassium Assignee: Unichem Laboratories Limited Filing date: 23/05/2007 Publication date: 27/03/2009 Status: Application abandoned 406/MUM/2008 Title: Extended release oral compositions of Losartan

	Assignee: Cadila Healthcare Limited Filing date: 28/02/2008 Publication date: 16/10/2009 Status: Application abandoned 1898/MUM/2008 Title: An improved process for preparing Losartan potassium Assignee: Alembic Ltd Filing date: 09/09/2008 Publication date: 13/08/2010 Status: Application abandoned 2265/MUM/2008 Title: A process for preparation of Losartan potassium form I Assignee: Alembic Ltd. Filing date: 21/10/2008 Publication date: 06/08/2010 Status: Application abandoned 3591/CHE/2010 Title: Process for Losartan potassium Assignee: Hetero Research Foundation Filing date: 29/11/2010 Publication date: 20/07/2012 Status: Application abandoned 2752/DEL/2011 Title: Aloe vera oil: a new skin permeation enhancer Assignee: Jamia Hamdard University Filing date: 22/09/2011 Publication date: 22/03/2013 Status: Application abandoned under section 21 1878/MUM/2013 Title: An improved process for the preparation of Losartan Assignee: Piramal Enterprises Limited Filing date: 28/05/2013 Publication date: 06/02/2015 Status: Application abandoned 2583/DEL/2013 Title: Pulsatile release dosage form of Losartan Assignee: Ranbaxy Laboratories Limited Filing Date: 02/09/2013 Publication date: 06/05/2016 Status: Application abandoned 907/MUM/2015 Title: Sustained release pharmaceutical compositions of Losartan potassium and process for preparation thereof Inventors: Pawar Harshal Ashok, Lalitha K.G. Filing date: 19/03/2015 Publication date: 24/04/2015 Status: Application abandoned

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/ .

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