

**Recommendations of the SEC meeting to examine COVID-19 related proposal under accelerated approval process made in its 156<sup>th</sup> meeting held on 06.05.2021 & 07.05.2021 at CDSCO, HQ New Delhi:**

Agenda No	File Name & Drug Name, Strength	Firm Name	Recommendation
<b>New Drug Division</b>			
1.	<p>1. F. No: IND/CT/21/000018 Molnupiravir capsules</p> <p>2. F. No: ND/MA/21/000044 Molnupiravir capsules</p> <p>3. F. No: ND/MA/21/000055 Molnupiravir capsules</p> <p>4. F. No: ND/MA/21/000053 Molnupiravir capsules</p>	<p>1. M/s Natco Pharma Limited</p> <p>2. M/s Optimus Pharma Pvt. Ltd</p> <p>3. M/s Dr. Reddy</p> <p>4. M/s MSN</p>	<p>Various protocols presented by the firms for Molnupiravir were deliberated by the committee.</p> <p>After detailed deliberation committee recommended as under:</p> <p>1. Every firm should conduct a Prospective, Randomized, Parallel, Multicenteric Phase III clinical trial in mild Covid patients.</p> <p>a) The objectives of the study should be as follows:</p> <p><b><u>Primary Objective:</u></b></p> <p>To evaluate the efficacy of Molnupiravir compared to standard of care in confirmed RT-PCR positive patients with Mild COVID-19.</p> <p><b><u>Secondary Objectives:</u></b></p> <p>To evaluate the safety of Molnupiravir compared to standard of care in confirmed RT-PCR positive patients with Mild COVID-19.</p> <p>b) The endpoints of the study should be as follows:</p> <p><b><u>Primary Endpoint:</u></b></p> <p>Rate of hospitalization from randomization up to Day 14</p> <p><b><u>Secondary Endpoints:</u></b></p> <ul style="list-style-type: none"> <li>• Rate of hospitalization from randomization up to Day 28</li> <li>• Proportion of patients with clinical improvement at end of treatment,</li> </ul>

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			<p>Day 10 and 14</p> <ul style="list-style-type: none"> <li>• Time to clinical improvement from randomization up to Day 14</li> <li>• Mortality rate at Day 14</li> <li>• Mortality rate at Day 28</li> <li>• Rate of SARS-CoV2 RT-PCR negativity in nasopharyngeal and/or oropharyngeal swab at end of treatment</li> <li>• Change in SARS CoV-2 viral load (Cycle Threshold (CT) value of RT-PCR test) from baseline to end of treatment</li> <li>• Incidence and severity of TEAEs (clinical and laboratory) during the study</li> <li>• Proportion of patients discontinued the study drug due to adverse events</li> </ul> <p>c) RTPCR test should be done at 5, 10 and 15 days of the study.</p> <p>d) Patients aged limit should be 18 to 60 years.</p> <p>e) Sample size should be atleast 1218 mild COVID patients to be randomized in 1:1 ratio into Test: Reference arm.</p> <p><b>Test Arm</b> Molnupiravir 800 mg (4 capsules of 200 administered orally every 12 hours for 5 days doses total) plus Standard of Care</p> <p><b>Reference Arm</b> Standard of Care</p> <p>2. Every firm should also conduct a Prospective, Randomized, Parallel, Multicenteric Phase II/III clinical trial in moderate Covid patients. The study should be conducted in two parts</p> <p>In part I, the study should be conducted in</p>

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			<p>100 patients and submit interim Clinical trial data to CDSCO for further consideration.</p> <p>a) The objective of the study should be as follows:</p> <p><b><u>Primary Objective:</u></b></p> <p>To evaluate the efficacy of Molnupiravir compared to standard of care in confirmed RT-PCR positive patients with Moderate Coronavirus Disease of 2019 (COVID-19).</p> <p><b><u>Secondary Objectives:</u></b></p> <p>To evaluate the safety of Molnupiravir compared to Standard of Care (SOC) in confirmed RT-PCR positive patients with Moderate Coronavirus Disease of 2019.</p> <p>The endpoints of the study should be as under:-</p> <p><b><u>Primary Endpoint:</u></b></p> <p>Proportion of patients with clinical improvement* at Day 14</p> <p>* Clinical Improvement is defined as 2-point decrease in Clinical Progression Scale as recommended by WHO</p> <p><b><u>Secondary Endpoints:</u></b></p> <ul style="list-style-type: none"> <li>• Proportion of patients with clinical improvement at Day 28</li> <li>• Time to clinical improvement from randomization up to 28 days</li> <li>• Mortality rate at Day 28</li> <li>• Rate of SARS-CoV2 RT-PCR negativity in nasopharyngeal and/or oropharyngeal swab at end of treatment (EOT), Day 14 and 28</li> <li>• Change in SARS CoV-2 viral load (Cycle Threshold (CT) value of RT-PCR test) from baseline to EOT, Day</li> </ul>

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			<p>14 and 28</p> <ul style="list-style-type: none"> <li>• Incidence and severity of TEAEs (clinical and laboratory) during the study</li> <li>• Proportion of patients discontinued the study drug due to adverse events</li> </ul> <p>The committee also recommended for grant of permission to conduct the trial in moderate patients as per the protocol presented, subject to the following conditions. The study should be conducted in two parts and termed as Phase II/III Clinical trial.</p> <p>a) In part I, the study should be conducted in 100 patients and submit interim Clinical trial data to CDSCO for further consideration.</p> <p>b) RTPCR test should be done at 5, 10 and 15 days of the study.</p> <p>c) Sample size should be atleast 1282 moderate COVID patients in randomized 1:1 ratio into Test: Reference arm.</p> <p><b>Test Arm</b> Molnupiravir 800 mg (4 capsules of 200 administered orally every 12 hours for 5 days doses total) plus Standard of Care</p> <p><b>Reference Arm</b> Standard of Care</p> <p>d) Patients aged limit should be 18 to 60 years.</p> <p>Accordingly the firm should submit revised Clinical trial protocol to CDSCO for approval.</p>
2.	<p>F. No: ND/MA/21/000050</p> <p>Molnupiravir 200mg, 400mg and 800mg capsules</p>	M/s Hetero	<p>In light of the earlier SEC recommendation dated 30.04.2021, firm presented revised Phase III Clinical Trial Protocol before the committee.</p> <p>After detailed deliberation committee recommended for grant of permission to</p>

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			<p>conduct the Phase III Clinical trial in mild patients as per the protocol, subject to the following conditions:</p> <p>a). RTPCR test should be done at 5, 10 and 15 days of the study.</p> <p>b) Patients aged limit should be 18 to 60 years.</p> <p>c) Sample size should be atleast 1218 mild COVID patients in randomized 1:1 ratio into Test: Reference arm.</p> <p>2. The committee also recommended for grant of permission to conduct the trial in moderate patients as per the protocol presented, subject to the following conditions. The study should be conducted in two parts and termed as Phase II/III Clinical trial.</p> <p>a) In part I, the study should be conducted in 100 patients and submit interim Clinical trial data to CDSCO for further consideration.</p> <p>b) RTPCR test should be done at 5, 10 and 15 days of the study.</p> <p>c) Sample size should be atleast 1282 moderate COVID patients in randomized 1:1 ratio into Test: Reference arm.</p> <p>d) Patients aged limit should be 18 to 60 years.</p> <p>Accordingly the firms should submit revised Clinical trial protocol to CDSCO for approval.</p>
<b>Biological Division</b>			
3.	X-11026/194/2020 BD  COVID-19 Hyper immune globuline	M/s Intas Pharmaceuticals	The firm has presented its Phase-II clinical Study report on COVID-19 Hyper Immune globulin in moderate and Severe COVID-19 patients and requested for emergency use authorisation of the product in COVID-19

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			<p>patients.</p> <p>After detailed deliberation, the committee did not recommend for approval of the product for emergency use due to lack of adequate efficacy data.</p>
4.	X-11026/188/2020 BD  Antiplatelet-Anti-Coagulant (Unfractionated Heparin-Serum Albumin conjugate)	M/s Cadila Pharmaceuticals Pvt. Ltd	<p>The firm presented its Phase-I clinical trial protocol on unfractionated Heparin-Serum Albumin conjugate (APAC) in healthy subjects.</p> <p>After detailed deliberation, the committee recommended as follows:</p> <ol style="list-style-type: none"> <li>1. All haematological parameters should be within limits w.r.t. the subjects enrolled in the study.</li> <li>2. Single dose and Multiple dose study should be conducted in same Healthy adults.</li> </ol> <p>However Committee also opined that Haematologist should also be invited during the next meeting for detailed deliberation on the proposed protocol.</p>
5.	X.11026/97/2021-BD	M/s Intas Pharmaceuticals Pvt. Ltd- Clinical Study Protocol	To be deliberated in next SEC (Covid-19) meeting.
<b>GCT Division</b>			
6.	CT/116/20 Online submission (22498)  Baricitinib	M/s. Spectra Hospital Services	To be deliberated in next SEC (Covid-19) meeting.
7.	CT/15/21 Online Submission (23729)  ATR-002	M/s. Clinixel Life Science	<p>In light of the observation of SEC, dated 24.02.2021, the firm presented their modified Phase II Clinical Trial Protocol.</p> <p><b>Risk-Benefit Assessment:</b> ATR-002 is a small molecule, it inhibits MEK1 and MEK2 (members of the Ras/Raf/MEK/ERK signaling pathway). ATR-002 is being developed for the treatment of viral infections, based on the finding that replication of some viruses in the host cells depends on an active Ras/Raf/MEK/ERK pathway.</p> <p><b>Innovation Vs Existing Therapy:</b></p>

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			<p>Based on these pre-clinical studies and the known mechanism of action, ATR-002 has emerged as a possible treatment option in patients suffering from COVID-19 lung disease resulting from infection with SAR-CoV-2. Therefore, the planned clinical trial of ATR-002 in Adult Hospitalized Patients with COVID-19 can potentially help in developing an effective antiviral agent against SARS- CoV-2.</p> <p><b>Unmet Need:</b></p> <p>To demonstrate the efficacy of ATR-002 versus placebo in addition to standard of care based on the clinical severity status in adult hospitalized patients with COVID-19.</p> <p>After detailed deliberation the committee recommended of the grant of permission for the conduct of Phase II Clinical Trial as per Clinical Trial Protocol presented.</p>
8.	CT/37/21 Online Submission (25352) SIR1-365	M/s JSS	To be deliberated in next SEC (Covid-19) meeting.
9.	CT/40/21 Online Submission (24830) Ensovibep (MP0420)	M/s IQVIA	To be deliberated in next SEC (Covid-19) meeting.
10.	CT/45/20 Online Submission (10623) BDB001	M/s. George Clinical India	To be deliberated in next SEC (Covid-19) meeting.
11.	CT/33/21 Online submission 24834 Hydroxy progestetene	M/s. CBCC Global Research.	<p>The firm has presented their Phase-II clinical Trial protocol before the committee.</p> <p>The committee observed that, the applicant could not show convincing in vivo efficacy data of the combination of Dexamethasone and Hydroxyprogesterone Caproate for inflammatory markers. Therefore, committee did not recommend the approval of the proposal for the conduct of Phase II Clinical Trial at this stage.</p>
12.	CT/115/20 Online Submission 22459 RBT-9/COVID-19	M/s JSS	Firm did not turn up for the presentation.

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13.	CT/08/21 Online Submission 23690  Carrimycin	M/s PAREXEL	To be deliberated in next SEC (Covid-19) meeting.
14.	CT/09/21 Online Submission 23712  BR11-196 and BR11-198	M/s PPD	In light of the observation of SEC, dated 23.03.2021 & 24.03.2021, the firm presented their Phase 2/3 Clinical Trial Protocol proposal. After detailed deliberation the committee recommended of the grant of permission for the conduct of the Phase 2/3 Clinical Trial as per Clinical Trial Protocol presented.
<b>FDC Division</b>			
15.	FDC/MA/201/000098  Each kit contains:  Part (A): 14 Zinc Acetate Tablets  Each film coated tablet contains:  Zinc Acetate (as Dihydrate) BP eq. to Elemental Zinc 50mg  Part (B): Doxycycline Capsules IP  Each hard gelatin capsule contains:  Doxycycline Hydrochloride IP eq. to Doxycycline 100mg  Part (C): Ivermectin Dispersible Tablets  Each uncoated dispersible tablet contains:  Ivermectin IP 12mg	M/s Windlas	Firm presented proposal of their combikit before the committee. After detailed deliberation, the committee opined that firm could not present any convincing clinical data in support of proposed combikit in respect of the proposal approval of dosage/strength of the various drugs. Hence, the committee did not recommend for the proposed combikit for the treatment of covid-19 at this stage.