

Recommendations of the SEC (Cardiovascular & Renal) made in its 109th meeting held on 07.09.2022 at CDSCO (HQ), New Delhi:

S.No.	File Name & Drug Name, Strength	Firm Name	Recommendations
New Drug Division			
1.	ND/MA/22/000078 Bempedoic Acid Tablet 180mg + Ezetimibe Tablet 10mg	M/s. MSN Labs	The firm presented their proposal for BE study protocol and Phase III CT Protocol before the committee. After detailed deliberation, the committee recommended for grant of permission to conduct the proposed BE study. The firm should initially present the BE study results before the committee for further consideration of Phase III CT protocol at that point of time.
2.	ND/MA/20/000097 Bempedoic Acid 180mg + Ezetimibe 10mg Tablet	M/s. Akums	The firm presented their proposal for grant of permission to manufacture and market Bempedoic Acid 180mg + Ezetimibe 10mg Tablet along with phase III clinical trial waiver. After detailed deliberation, the committee noted that the firm has not presented any new justification for the waiver of the Phase III clinical trial. Hence, the committee reiterated its earlier recommendation dated 09.06.2022 and 10.06.2022.
SND Division			
3.	SND/MA/22/000083 Polystyrene Sulphonate Jelly 20% w/w	M/s. Pharose Remedies	The firm didn't turn up for presentation.
4.	SND/MA/21/000482 Ticagrelor SR Tablets 120/180mg	M/s. Theon Pharma	The proposal was deferred as per request of the firm.
FDC Division			
5.	FDC/MA/19/000106 Efonidipine Hydrochloride Ethanolate 20mg/20mg/40mg + Telmisartan IP 20mg/40mg/40mg	M/s. Zuventus Healthcare Ltd.	As per the condition mentioned in the permission dated 30.12.2021, the firm presented the Phase IV CT study Protocol before the committee. After detailed deliberation, the committee opined that:

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	uncoated bilayered tablet		<ol style="list-style-type: none"> 1. The firm should include all the investigations which were done in Phase-III CT study. 2. The sample size should be statistically significant. 3. Different study centers should be taken for the Phase IV CT study.
6.	FDC/MA/22/000096 Clopidogrel bisulphate eq. to Clopidogrel 75mg + Atorvastatin Calcium eq. to Atorvastatin 40mg tablets	M/s. Pure & Cure Healthcare Pvt. Ltd.	The committee noted that the proposal had already been deliberated.
7.	FDC/MA/22/000094 Bempedoic acid 180mg/180mg/180mg /180mg + Atorvastatin Calcium eq. to Atorvastatin 10mg/20mg/40mg/80mg tablets	M/s. Exemed Pharmaceuticals	<p>In light of earlier SEC recommendation dated 09.06.2022 & 10.06.2022, the firm presented the bioequivalence report before the committee. The firm also presented the Phase III clinical trial data generated with the concomitant use of Atorvastatin & Bempedoic acid.</p> <p>After detailed deliberation, the committee recommended for grant of permission for manufacture and market of the proposed FDC for the higher strength only i.e. Atorvastatin Calcium eq. to Atorvastatin 80mg + Bempedoic acid 180mg tablets with the condition to submit the Phase IV clinical trial protocol within 03 months from the date of approval.</p>
8.	FDC/MA/22/000241 Chlorthalidone IP 6.25mg/12.5mg + Cilnidipine 5mg/10mg + Bisoprolol Fumarate 5mg/10mg tablets	M/s. Windlas Biotech Ltd.	The proposal was deferred as per request of the firm.
9.	FDC/MA/22/000248 Bisoprolol Fumarate IP 2.5mg/5mg/10mg + Telmisartan IP 20mg/40mg/80mg + Chlorthalidone IP 6.25mg / 12.5mg /12.5mg uncoated	M/s. Windlas Biotech	<p>The firm presented their proposal for proposed FDC. After detailed deliberation, the committee opined that:</p> <ol style="list-style-type: none"> 1. The firm should present the justification and essentiality for the proposed FDC. 2. The dosing schedule and duration was

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	tablet		<p>not defined for proposed FDC.</p> <p>3. Scientific justification with rationality along with published literature in peer reviewed journals in support of FDC to be presented</p> <p>4. Justification for proposed indication was not presented.</p> <p>In view of above, the committee recommended that the firm should present the justification for aforesaid points before the SEC for further consideration.</p>
10.	FDC/MA/22/000242 Bisoprolol Fumarate IP 5mg/2.5mg + Cilnidipine IP 10mg/10mg tablets	M/s. Ajanta Pharma Ltd.	The proposal was deferred for next meeting.
11.	FDC/MA/22/000234 Bisoprolol Fumarate IP 5mg/2.5mg + Cilnidipine IP 10mg/10mg tablets	M/s. Windlas Biotech	<p>The firm presented their proposal along with proposed protocol before the committee.</p> <p>After detailed deliberation, the committee noted that the firm presented incomplete protocol.</p> <p>In view of above, the committee recommended that firm should present complete protocol with relevant details before SEC for further deliberation.</p>
12.	FDC/MA/21/000193 Bisoprolol 40mg/40mg + Telmisartan 2.5mg/5mg tablets	M/s. Windlas Biotech Ltd.	<p>In light of earlier SEC recommendation dated 07.09.2021 & 08.09.2021, the firm presented the bioequivalence study report and Phase III CT report before the committee.</p> <p>After detailed deliberation, the committee recommended that firm should submit the raw data of study reports and same should be circulated to all experts for review and their comments.</p>
13.	FDC/MA/21/000134 Bisoprolol 5mg/2.5mg + Telmisartan 40mg/40mg tablets	M/s. Micro Labs	In light of earlier SEC recommendation dated 25.08.2022, the firm presented the justification on sample size calculation. After detailed deliberation, the committee recommended for grant of permission to manufacture and market the proposed FDC.

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GCT Division			
14.	CT/33/22 Online Submission (31451) Sibeprenlimab	M/s. George Clinical	<p>In light of earlier SEC recommendation dated 28.07.2022, the firm presented the Phase I and Phase II study data along with proposed Phase 2/3 open label clinical trial protocol before the committee.</p> <p>After detailed deliberation, the committee opined that –</p> <p>“Open label extension” extension study usually follow Phase-III clinical trial in most of the cases while in the present situation it is being asked following at least one Phase-II study. Also, most of the time, OLE study is planned at the time of start of main study to which it follows, and this is explained at the start of main study itself to subject.</p> <p>It is usually done for assessing long-term safety while in present protocol, all secondary end points are for assessing efficacy of the test drug and also even the title of study is also including efficacy.</p> <p>Phase-II study has not shown any benefit over the placebo for improving eGFR while in term of proteinuria, there is rebound after decrease is proteinuria by > 30% over time, though the presenter is explaining these results by limited data set of interim analysis. OLE study is being planned while the results will remain blinded and there is no provision of unblinding the results before enrolling patients in OLE study. In this situation, patients who are responder to placebo, will be given drug unnecessarily, which is unjustified.</p> <p>Inclusion criteria states that subjects will be enrolled in OLE study who “in the opinion of the investigator, could potentially benefit from treatment with sibeprenlimab”.</p> <p>In opinion of technical experts, without unblinding, how can investigator assess benefit of the test drug in an individual subject.</p> <p>Also, “Subject is judged by the investigator or the medical monitor to be inappropriate for the trial” as an exclusion criteria is an open ended statement. Similar is exclusion criteria on</p>

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			<p>safety based on investigator judgement.</p> <p>The two studies to which this OLE study is expected to follow are 417-201-00007, in which main cohort has eGFR > 30 ml and VIS649-201, in which eGFR is > 45 ml/min. However, in OLE study, eGFR planned is upto 20 ml/min, which is significantly lower than both the main studies.</p> <p>Lastly, OLE study is being planned while a phase-III study has already approved to assess safety and efficacy in large number of patients with longer follow-up of 24 months.</p> <p>In view of above issues, this proposed OLE study is not recommended.</p>
15.	<p>CT/56/22 Online Submission (32776)</p> <p>AZD9977 &Dapagliflozin</p>	M/s. Parexel	<p>The applicant presented Phase IIb clinical trial protocol no. D6402C00001, amendment 6 version 7.0 dated 02/02/2022 before the committee.</p> <p>Risk versus benefit to the patients- The safety profile of the study drug from preclinical and clinical studies justify the conduct of the trial.</p> <p>Innovation vis-a-vis existing therapeutic option- The proposed study is to evaluate the efficacy, safety and tolerability of Oral AZD9977 and Dapagliflozin treatment in patients with heart failure and chronic kidney disease.</p> <p>Unmet medical need- The test drug may be alternative treatment option for patients with heart failure and chronic kidney disease.</p> <p>After detailed deliberation, the committee opined that only one disease either chronic kidney disease (CKD) or heart failure should be studied in proposed phase IIb study. Accordingly, the committee recommended that the applicant should submit revised protocol.</p>
Medical Device Division			
16.	<p>IMP/MD/2020/24773</p> <p>Syplicity SpyratTM Renal Denervation System</p>	<p>M/s. India Medtronic Pvt. Ltd.</p>	<p>In light of earlier SEC recommendation dated 09.09.2020 & 10.09.2020, the firm presented their proposal before the committee.</p> <p>After detailed deliberation, the committee recommended for grant of import and</p>

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			<p>market permission of the proposed device -multi electrode renal denervation catheter (Symplicity Spyral) with the condition that the firm should conduct the Phase IV clinical investigation.</p> <p>Accordingly, the firm should submit the Post Marketing (Phase IV) clinical investigation protocol to the CDSCO for further review by the committee.</p>
17.	<p>29/Misc./03/2022-DC(135)</p> <p>MLS/Evermine 50 EES-1</p>	M/s. Meril life sciences Pvt. Ltd.	The firm didn't turn up for presentation.