Nil

File No.FDC/MA/23/000063
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(FDC Division)

Tele. No.:011-23236965
Fax No. :011-23236973

FDA Bhawan, Kotla Road
New Delhi-110002

Dated: 02 NOV 2023

To,

M/s. Exemed Pharmaceuticals,
133/1 & 133/2, GIDC Selves Road,
Vapi-396195 Gujarat (India).

Subject: Permission to conduct Phase III Clinical trial with the FDC of Dapagliflozin Propanediol monohydrate eq. to Dapagliflozin 10mg + Metoprolol Succinate IP eq. to Metoprolol Tartrate (as extended release) 50mg film coated bilayered tablet (Vide protocol no. CT/2023/11, version no. 02, dated 04.08.2023)-regarding.

Dear Sir,

With reference to your online application submitted in Form CT-21 on dated 10.03.2023 please find enclosed herewith the "permission to conduct clinical trial study of new drug" bearing no. **FDC-CT-06-55/2023** under the provision of Drugs and Cosmetics Act and Rules. The permission is subject to the conditions mentioned below.

Kindly acknowledge receipt to this letter and its enclosures.

Yours faithfully,

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

CONDITIONS OF PERMISSION

I. Clinical trial at each site shall be initiated after approval of the clinical trial protocol and other related documents by the Ethics Committee of that site, registered with the Central Licencing Authority under rule 8;

II. Where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Ethics Committee of another trial site; or an independent Ethics Committee for clinical trial constituted in accordance with the provisions of rule 7:

   i. Provided that the approving Ethics Committee for clinical trial shall in such case be responsible for the study at the trial site or the centre, as the case may be:
   ii. Provided further that the approving Ethics Committee and the clinical trial site or the bioavailability and bioequivalence centre, as the case may be, shall be located within the same city or within a radius of 50 kms of the clinical trial site;

III. In case an ethics committee of a clinical trial site rejects the approval of the protocol, the details of the same shall be submitted to the Central Licensing Authority prior to seeking approval of another Ethics Committee for the protocol for conduct of the clinical trial at the same site;

IV. The Central Licencing Authority shall be informed about the approval granted by the Ethics Committee within a period of fifteen working days of the grant of such approval;

V. Clinical trial shall be registered with the Clinical Trial Registry of India maintained by the Indian Council of Medical Research before enrolling the first subject for the trial;

VI. Clinical trial shall be conducted in accordance with the approved clinical trial protocol and other related documents and as per requirements of Good Clinical Practices Guidelines and the provisions of these rules;

VII. Status of enrolment of the trial subjects shall be submitted to the Central Licencing Authority on quarterly basis or as appropriate as per the duration of treatment in accordance with the approved clinical trial protocol, whichever is earlier;

VIII. Six monthly status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Central Licencing Authority electronically in the SUGAM portal;

IX. In case of termination of any clinical trial the detailed reasons for such termination shall be communicated to the Central Licencing Authority within thirty working days of such termination;

X. Any report of serious adverse event occurring during clinical trial to a subject of clinical trial, shall, after due analysis, be forwarded to the Central Licencing Authority, the chairperson of the Ethics Committee and the institute where the trial has been conducted within fourteen days of its occurrence as per Table 5 of the Third Schedule and in compliance with the procedures as specified in Chapter VI;

XI. In case of injury during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of the receipt of order issued by Central Licencing Authority in accordance with the provisions of the said Chapter;

XII. In case of clinical trial related death or permanent disability of any subject of such trial during the trial, compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of receipt of the order issued by the Central Licencing Authority in accordance with the provisions of the said Chapter;

XIII. The premises of the sponsor including his representatives and clinical trial sites, shall be open for inspection by officers of the Central Licencing Authority who may be accompanied by officers of the State Licencing Authority or outside experts as authorised by the Central Licencing Authority, to verify compliance of the requirements of these rules and Good Clinical Practices Guidelines, to inspect, search and seize any record, result, document, investigational product, related to clinical trial and furnish reply to query raised by the said officer in relation to clinical trial;

XIV. Where the new drug or investigational new drug is found to be useful in clinical development, the sponsor shall submit an application to the Central Licencing Authority for permission to import or manufacture for sale or for distribution of new drug in India, in accordance with Chapter X of these rules, unless otherwise justified;

XV. The laboratory owned by any person or a company or any other legal entity and utilised by that person to whom permission for clinical trial has been granted used for research and development, shall be deemed to be registered with the Central Licensing Authority and may be used for test or analysis of any drug for and on behalf of Central Licensing Authority;

XVI. The Central Licencing Authority may, if considered necessary, impose any other condition in writing with justification, in respect of specific clinical trials, regarding the objective, design, subject population, subject eligibility, assessment, conduct and treatment of such specific clinical trial;

XVII. The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.

XVIII. It may kindly be noted that merely granting permission to conduct Clinical trials/Bioavailability or Bioequivalence study with the drug does not convey or imply that, based on the Clinical trial data/ Bioavailability or Bioequivalence study data generated with the drug, permission to market this drug in the country will automatically be granted to you.

XIX. The formulation intended to be used in the clinical trial study shall be manufactured under GMP conditions using validated procedures.

XX. **The firm should submit Phase III CT study report to CDSCO for review by the committee.**

FORM CT-06

(See rules 22, 25, 26, 29 and 30)

PERMISSION TO CONDUCT CLINICAL TRIAL OF NEW DRUG ~~OR INVESTIGATIONAL NEW DRUG~~

Permission no.: FDC-CT-06-55/2023

1. The Central Licencing Authority hereby permits **M/s. Exemed Pharmaceuticals, 133/1 & 133/2, GIDC Selves Road, Vapi-396195 Gujarat (India) Telephone No. 912606617700 Fax 912606617799** to conduct clinical trial of the new drug or investigational new drug as per protocol number **(Vide protocol no. CT/2023/11, version no. 02, dated 04.08.2023)** in the below mentioned clinical trial sites.
2. Details of new drug or investigational new drug and clinical trial site [As per Annexure].
3. This permission is subject to the conditions prescribed in part A of Chapter V of the New Drugs and Clinical Trials Rules, 2019 under the Drugs and Cosmetics Act, 1940.

Place: New Delhi

Date: .....

02 NOV 2023

Central Licencing Authority

Stamp

Dr. RAJEEV SINGH RAGHUVANSHI
Drugs Controller General (India)
Central Drugs Standard Control Organisation
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India
FDA Bhawan, Kotla Road,
New Delhi-110002

Annexure:

Details of new drug or investigational new drug:

Names of the new drug or investigational new drug:	Dapagliflozin Propanediol monohydrate eq. to Dapagliflozin 10mg + Metoprolol Succinate IP eq. to Metoprolol Tartrate (as extended release) 50mg film coated bilayered tablet
Therapeutic class:	Antidiabetic and Antihypertensive
Dosage form:	Tablets
Composition:	Each film coated tablet contains: Dapagliflozin Propanediol monohydrate eq. to Dapagliflozin .....10mg Metoprolol Succinate IP eq. to Metoprolol Tartrate .....50mg (as extended release)
Indications:	It is indicated in patient with Heart Failure with Reduced Ejection Fraction(HFrEF)

Details of clinical trial site:

Names and address of clinical trial site:	As per annexure- A
Ethics committee details:	As per annexure- A
Name of principal investigator:	As per annexure- A

Annexure-A

Permission no.: FDC-CT-06-55/2023

S. No.	Name of PI	Site Name	Ethics Committee Name, Address & EC registration No
1.	Dr. Abhishek Sachdeva	Department of Cardiology, Swaroop Rani Motilal Nehru Medical College, Prayagraj-211001, Uttar Pradesh	Institutional Ethics Committee, Motilal Nehru Medical College, George Town, Prayagraj, Allahabad-211002, Uttar Pradesh. ECR/922/Inst/UP/2017/RR22
2.	Dr. Sanjay Kumar Sharma	Maharaja Agrasen Superspeciality Hospital, Central Spine, Agrasen Aspatal Marg, Sector 7, Vidyadhar Nagar, Jaipur-302039, Rajasthan.	Institutional Ethics Committee, Maharaja Agrasen Superspeciality Hospital, Central Spine, Agrasen Aspatal Marg, Sector 7, Vidyadhar Nagar, Jaipur-302039, Rajasthan. ECR/1222/Inst/RJ/2019/RR-22
3.	Dr. Ashish Kumar Agarwal	Department of Cardiology, Jawahar Lal Nehru (J.L.N) Medical College, Kala Bagh, Ajmer-305001, Rajasthan.	Institutional Ethics Committee, Jawahar Lal Nehru Medical College, Kala Bagh, Ajmer-305001, Rajasthan ECR/1156/Inst/RJ/2018/RR22
4.	Dr. Rajesh Kumar Pandey	Chirayu Hospital, (A Unit of KSCH Pvt. Ltd), Kalwar Road, Hathoj, Jaipur-302012, Rajasthan	Institutional Ethics Committee, Chirayu Hospital, (A Unit of KSCH Pvt. Ltd), Kalwar Road, Hathoj, Jaipur-302012, Rajasthan ECR/1582/Inst/RJ/2021
5.	Dr. Bhagya Narayan Pandit	Dr. Ram Manohar Lohia Hospital, Postgraduate Institute of Medical Education and Research, Baba Kharak Singh Road, Near Gurudwara Bangla Sahib, Type III, Connaught Place, New Delhi-110001.	Ethics Committee, PGIMER, Dr. Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, Near Gurudwara Bangla Sahib,Type III, Connaught Place, New Delhi-110001. ECR/78/Inst/DL/2013/RR-19
6.	Dr. Dipak Ranjan Das	Department of Cardiology, Srirama Chandra Bhanja Medical College and Hospital, Cuttack-753007, Odisha	Institutional Ethics Committee, Srirama Chandra Bhanja Medical College and Hospital, Cuttack-753007, Odisha ECR/84/Inst/OR/2013/RR-20
7.	Dr. Jayanta Saha	Department of Cardiology, Medical College and Hospital, Kolkata, MCH Building, 4th Floor, 88 College Street, Kolkata-700073, West Bengal.	Institutional Ethics Committee for Human Research, Medical College and Hospital, Kolkata, 88, College Street, Kolkata-700073, West Bengal. ECR/287/Inst/WB/2013/RR-19
8.	Dr. Swapan Kumar Halder	NRS Medical College & Hospital, 138, Acharya Jagdish Chandra Bose Road, Sealdah, Raja Bazar, Kolkata, West Bengal 700014	Institutional Ethics Committee, NRS Medical College & Hospital, 138, Acharya Jagdish Chandra Bose Road, Sealdah, Raja Bazar, Kolkata, West Bengal 700014 ECR/609/Inst/WB/2014/RR-20
9.	Dr. Sanjay Vithalrao Desai	Prakash Institute of Medical Sciences & Research (PIMS&R), Urun-Islampur, Islampur-Sangali Road, Islampur, Tal-Walwa, Dist-Sangali-415409, Maharashtra.	Prakash Medical College Institutional Ethics Committee, Prakash Institute of Medical Sciences & Research (PIMS&R), Urun-Islampur, Islampur-Sangali Road, Islampur, Tal-Walwa, Dist-Sangali-415409, Maharashtra, ECR/1052/Inst/MH/2018/RR21

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10	Dr. Kulin Sheth	Aatman Hospital, 5, Anveshan Row House, Bopal Gam BRTS, Bopal-Ghuma Road, Bopal, Ahmedabad-380058, Gujarat.	Institutional Ethics Committee, Aatman Hospital, 5, Anveshan Row House, Opp. Umiya Mata Mandir, Bopal-Ghuma Main Road, Bopal, Ahmedabad-380058, Gujarat. ECR/1565/Inst/GJ/2021
11	Dr. Dhaiwat Shukla	Sheth Vadilal Sarabhai General Hospital, Nr. Ellisbridge, Paldi, Ahmedabad-380006, Gujarat.	Institutional Ethics Committee Aatman Hospital, Aatman Hospital, 5, Anveshan Row House, Opp. Umiya Mata Mandir, Bopal-Ghuma Main Road, Bopal, Ahmedabad-380058, Gujarat ECR/1565/Inst/GJ/2021
12	Dr. Krishna Mala Konda Reddy P	Department of Cardiology, Osmania Medical College & General Hospital, Afzalgunj, Hyderabad, Telangana-500012.	Upgraded Department of Pathology, Osmania Medical College & General Hospital, Afzalgunj, Hyderabad, Telangana-500012, India. Or Ampath Central Reference Laboratory, Nallagandla, Serilingampally, Hyderabad-500019, Telangana. ECR/300/Inst/AP/2013/RR19
13	Dr. Jenny Madhuri Gudivada	Department of Cardiology, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam-530002, Andhra Pradesh.	Institutional Ethics Committee, King George Hospital, Maharanipeta, Collector Office Junction, Visakhapatnam-530002, Andhra Pradesh. ECR/197/Inst/KGH/2013/RR20

Place: New Delhi

Date: .....

02 NOV 2023

Central Licencing Authority

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Dr. RAJEEV SINGH RAGHUVANSHI
Drugs Controller General (India)
Central Drugs Standard Control Organization
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India
FDA Bhawan, Kotla Road,
New Delhi (India)

S. No	File Name & Drug Name, Strength	Firm Name	Recommendations
	salt complex 50mg (24mg and 26mg), 100mg (49mg and 51mg) &200mg (97mg and 103mg) tablet		
4.	FDC/MA/23/000288 Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin + Bisoprolol Fumarate IP (10mg+1.25mg, 10mg+2.5mg, 10mg+5mg & 10mg+10mg) tablet	M/s. Exemed Pharmaceutical	The firm did not turn up for presentation.
5.	FDC/MA/19/000106 Efonidipine Hydrochloride Ethanolate +Telmisartan IP (20mg+40mg/ 40mg+40mg) uncoated bilayered tablets	M/s. Zuventus Healthcare Ltd.	In light of the condition mentioned in permission in Form CT-23 dated 30.12.2021, the firm presented the Phase IV clinical trial protocol for FDC of Efonidipine Hydrochloride Ethanolate 40mg + Telmisartan IP 40 mg tablets before the committee. After detailed deliberation, the committee recommended for conduct of the Phase IV clinical trial. The firm should submit the Phase IV clinical trial report to CDSCO for further review by the committee.
6.	FDC/MA/20/000077 Azelnidipine + Metoprolol (SR) 8mg/8mg/16mg/16mg + 25mg/ 50mg/25mg/50mg tablet	M/s. Akums Drugs & Pharmaceuticals Ltd.	In light of the SEC recommendation dated 07.06.2023, the firm presented their proposal along with clarification/justification w.r.t. clinical trial result. After detailed deliberation, the committee opined that the firm should submit raw data of the CT to CDSCO for review by the committee.
7.	FDC/MA/23/000063 Dapagliflozin Propanediol monohydrate 5mg/5mg/10mg/10mg + Metoprolol Succinate IP eq. to	M/s. Exemed Pharmaceuticals	In light of the SEC recommendation dated 06.07.2023 & 07.07.2023, the firm presented their proposal along with BE report & revised Phase III clinical trial protocol with change in indication before the committee. The committee noted that CDSCO has already issued BE & CT NOC on 25.08.2023. However firm has not

S. No	File Name & Drug Name, Strength	Firm Name	Recommendations
	Metoprolol tartrate (ER) 25mg/50mg/25mg/50 mg tablets		initiated Phase III CT study. After detailed deliberation, the committee considered BE report and recommended for grant of permission to initiate the Phase III CT with the condition that Guideline Directed Medical Therapy (GDMT) for heart failure as a concomitant medication to be allowed for all the subjects. Accordingly, the firm should submit Phase III CT study report to CDSCO for review by the committee.
8.	FDC/MA/23/000293 Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin + Telmisartan (10mg+40mg/ 10mg+80mg) film coated tablet	M/s. Eris Lifesciences Limited	The firm presented their proposal along with BE study protocol & Phase III clinical trial protocol before the committee. After detailed deliberation, the committee recommended for grant of permission to conduct the BE study & Phase III clinical trial. The result of the BE study should be presented for review by SEC before initiation of the Phase III clinical trial.
Medical Device Division			
9.	CI/MD/2021/50669 Pericardial Bioprosthesis Dafodil (1st Brand), Dafodil Neo (2nd Brand), Flomeo (3rd Brand), Freesia (4th Brand)	M/s. Meril Life Sciences Private Limited	The firm presented the 100 patients data as recommended by the SEC (cardiovascular & Renal) dated 08.02.2023 After detailed deliberation, the committee recommended to present the data in the SEC meeting alongwith (cardiothoracic) surgeon.