सत्यमेव जयते

Government of India
Central Drugs Standard Control Organisation(Headquarter)
(Directorate General of Health Services)
FDA Bhavan, ITO, Kotla Road
New Delhi - 110002 (Delhi)
Phone No.: 91-11-23216367
Fax No.: 91-11-23236973
E-Mail: dci@nic.in

File No. BIO/CT/21/000052 Dated 09-Jan-2023

To,
M/s Zydus Lifesciences Limited(Formerly Cadila Healthcare Limited),
Plot Survey No. 23, 25/P, 37,40/P, 42, To 47
Sarkhej-Bavla N.H. No-8A, Opposite Ramdev Masala,
Village Changodar, Tal.Sanand
Ahmedabad (India) – 382213

Subject: Application for grant of permission to conduct Phase IV clinical trial entitled –" A phase IV, prospective, multicentre, open-label,single arm study to evaluate the safety and efficacy of Trastuzumab Emtansine (UJVIRATM; Cadila Healthcare Ltd) in HER2-Positive Metastatic Breast Cancer Patients" as per Protocol TDM1.21.001,Version 04, Dated 08 Feb 2022- regarding

Ref.:Your Application No BIO/CT04/FF/2021/25033 dated 16-APR-2021

Sir,

With reference to your Application No BIO/CT04/FF/2021/25033 dated 16-APR-2021, please find enclosed herewith the permission in Form CT-06 for conduct of subject Phase IV clinical trial under the provisions of New Drugs and Clinical Trial Rules, 2019.

The permission granted by the Central Licensing Authority to conduct clinical trial under this Chapter shall be subject to following conditions, namely:

(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 Licensing 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:
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:
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 Licensing 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 Licensing 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 Licensing 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 Licensing 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 Licensing 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 Licensing Authority within thirty working days of the receipt of order issued by Central Licensing 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 Licensing Authority within thirty working days of receipt of the order issued by the Central Licensing 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 Licensing Authority who may be accompanied by officers of the State Licensing Authority or outside experts as authorised by the Central Licensing 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) 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;

(XV) The Central Licensing 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;

(XVI) The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.

Yours faithfully,

VENUGOPAL G SOMANI

(Dr. V.G. Somani)
Drugs Controller General (India)

Digitally signed by VENUGOPAL G SOMANI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL ORGANIZATION, ou=DRUGS CONTROLLER GENERAL (INDIA), pseudonym=112046a34e21727bacb25574e3113c, postalCode=110002, st=DELHI, serialNumber=e97f241aa0c0bba41522525ffca0705074b4997e6b2f4b5c8d81cf282adeaf5d, cn=VENUGOPAL G SOMANI
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FORM CT-06

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

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

The Central Licencing Authority hereby permits M/s Zydus Lifesciences Limited(Formerly Cadila Healthcare Limited),Plot Survey No. 23, 25/P, 37,40/P, 42, To 47 Sarkhej-Bavla N.H. No-8A, Opposite Ramdev Masala, Village Changodar, Tal.Sanand, Ahmedabad (India) – 382213, India to conduct clinical trial of the new drug or investigational new drug Phase IV study titled –" A phase IV, prospective, multicentre, open-label,single arm study to evaluate the safety and efficacy of Trastuzumab Emtansine (UJVIRATM; Cadila Healthcare Ltd) in HER2-Positive Metastatic Breast Cancer Patients" as per Protocol TDM1.21.001,Version 04, Dated 08 Feb 2022 in the below mentioned clinical trial sites.

2. Details of 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: 09-Jan-2023

VENUGOPAL G SOMANI

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Date: 2023.01.09 15:42:02 +05'30'

(Dr. V.G. Somani)
Drugs Controller General (India)
Central Licencing Authority

Annexure:

Details of new drug or investigational new drug:

<table>
<tr><td>Name of the new drug :</td><td>Trastuzumab Emtansine 100 mg and 160 mg vial (r-DNA origin)</td></tr>
<tr><td>Dosage form:</td><td>Lyophilized Powder for concentrate for solution for Intravenous infusion in Vial</td></tr>
<tr><td>Composition:</td><td>Each Lyophilized vial contains:
<table>
<tr><th>Name of Ingredients</th><th>For 100 mg /Vial quantity in mg</th><th>For 160 mg/Vial quantity in mg</th></tr>
<tr><td>Trastuzumab Emtansine(r-DNA origin) (In-house)</td><td>100</td><td>160</td></tr>
<tr><td>Succinic acid (IP/NF)</td><td>5.9</td><td>9.44</td></tr>
<tr><td>Sucrose (IP/USP/NF)</td><td>300</td><td>480</td></tr>
<tr><td>Polysorbate 20 (IP/NF)</td><td>1.0</td><td>1.6</td></tr>
<tr><td>Sodium hydroxide (IP/NF)</td><td>q.s to pH adjustment</td><td>q.s to pH adjustment</td></tr>
<tr><td>Water For Injection (IP/USP)</td><td>q.s</td><td>q.s</td></tr>
<tr><td>Reconstitution volume with Sterile water for Injection</td><td>5ml</td><td>8ml</td></tr>
</table></td></tr>
<tr><td>Indication:</td><td>1) Metastatic Breast Cancer (MBC) for the treatment of HER2- positive, unresectable locally advanced or metastatic breast cancer, in patients who had previously received trastuzumab and a taxane, separately or in combination. Such patients should have either i) received prior therapy for locally advanced or metastatic disease, or ii) developed a disease recurrence during or within six months of completing adjuvant therapy.
2) Early Breast Cancer (EBC) for the adjuvant treatment of patients with HER2-positive early breast cancer with residual invasive disease in the breast and/or lymph nodes after receiving neo-adjuvant taxane based and HER2-targeted therapy</td></tr>
</table>

Details of clinical trial site:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1	Unique Hospital-Multispecialty & Research Institute, Opp. Kiran Motor, Nr. Canal,Civil Hospital Char Rasta-Sosyo Circle Lane, Off Ring Road, Surat-395002, Gujarat	Ethics Committee Unique Hospital-Multispecialty & Research Institute, Opp. Kiran Motor, Nr. Canal, CivilHospital Char Rasta-Sosyo Circle Lane, Off Ring Road, Surat-395002, Gujarat, India EC Reg no: ECR/595/Inst/GJ/2014/RR-20	Dr Tanveer Maksud
2	Erode Cancer Centre Pvt.Ltd 1/393,Velavan Nagar, Perundurai Road,Thindal, ERODE, Tamil Nadu-638012 Indi	Institutional Ethics Committee, Erode Cancer Centre1/393, Velavan Nagar, Perundurai Road,Thindal, ERODE, Tamil Nadu-638012 India EC Reg no: ECR/319/Inst/TN/2013/RR-19	Dr Kandappan Velavan
3	Sparsh Hospital & critical care Ltd, A-407, Saheednagar, Bhubaneswar Odisha-751007	Institutional Ethics Committee sparsh Hospital, Sparsh Hospital & critical care Private Ltd, Plot no-A/407, Saheednagar, Bhubaneswar-751007 Odisha, India, EC Reg no: ECR/68/Inst/OR/2013/RR-19	Dr. Ghanshyam Biswas
4	HCG Cancer Centre,Sola Science City Road,Nr. Sola Bridge, S.G Highway, Ahmedabad-380060, Gujarat, India	HCG Multispeciality Ethics Committee, HCG Multi Speciality Hospital, Mithakhali, Ellisbridge,Ahmedabad-380006 EC Reg no: ECR/92/Inst/GJ/2013/RR-19	Dr. Manasi Shah