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/24/000130 Dated: 12-03-2025

To,

M/s. Hetero Biopharma Limited,
Sy.No 458 (part), TSIIC formulation SEZ, Polepalle Village
Jadcherla Mandal, Mahabubnagar District, Telangana-509301

Subject: Application for grant of permission to conduct Phase I/III clinical trial entitled – "A Prospective, Randomized, Double Blind, Multiple Dose, Multicenter, Active Controlled, Comparative, Parallel Study to Evaluate the Efficacy, Safety, Pharmacokinetic and Immunogenicity of Intravenous Infusion of Hetero-Pembrolizumab (Hetero Biopharma Ltd, India) and Reference Medicinal Product (Pembrolizumab, Merck Sharp & Dohme B.V) in Patients with Non-Squamous Type of Metastatic Non-Small Cell Lung Carcinoma (mNSCLC)" as per Protocol no. HCR/III/PEMBNSCLC/06/2024 Version No. 1.0 dated 16.08.2024- regarding

Ref. No.: Your Application No. BIO/CT04/FF/2024/45884 dated 11.10.2024 -reg

Sir,

With reference to your application No BIO/CT04/FF/2024/45884 dated 11.10.2024, please find enclosed herewith the permission in Form CT-06 for conduct of subject 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) All clinical study investigators should be Medical Oncologist.
(II) Clinical trial sites should be geographically distributed including Government sites.
(III) CSR shall be submitted to this office after completion of trial.
(IV) 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
(V) 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;

(VI) 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;

(VII) 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;

(VIII) 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.

(IX) 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.

(X) 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;

(XI) 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.

(XII) 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.

(XIII) 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.

(XIV) 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.

(XV) 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.

(XVI) 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 authorized 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.

(XVII) 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.

(XVIII) 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.

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

(XX) It may kindly be noted that merely granting permission to conduct clinical trial with the drug does not convey or imply that based on the clinical trial data generated with the drug permission to market this drug in the country will automatically be granted to you.

Yours faithfully,

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
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(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)
Licensing Authority

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 Licensing Authority hereby permits M/s. Hetero Biopharma Limited, Sy.No 458 (part), TSIIC formulation SEZ, Polepalle Village Jadcherla Mandal, Mahabubnagar District, Telangana-509301 to conduct Phase I/III clinical trial titled- "A Prospective, Randomized, Double Blind, Multiple Dose, Multicenter, Active Controlled, Comparative, Parallel Study to Evaluate the Efficacy, Safety, Pharmacokinetic and Immunogenicity of Intravenous Infusion of Hetero-Pembrolizumab (Hetero Biopharma Ltd, India) and Reference Medicinal Product (Pembrolizumab, Merck Sharp & Dohme B.V) in Patients with Non-Squamous Type of Metastatic Non-Small Cell Lung Carcinoma (mNSCLC)" as per Protocol no. HCR/III/PEMBNSCLC/06/2024 Version No. 1.0 dated 16.08.2024 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.

4**.** It may kindly be noted that merely granting permission to conduct clinical trial with the drug does not convey or imply that based on the clinical trial data generated with the drug permission to market this drug in the country will automatically be granted to you.

Place: New Delhi
Date: 12-03-2025

RAJEEV SINGH RAGHUVANSHI

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Date: 2025.03.17 10:31:45 +05'30'

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)
Central Licensing Authority

Annexure:

Details of new drug or investigational new drug:

<table>
<tr><td>Names of the new drug or investigational new drug:</td><td>Pembrolizumab concentrate for solution for Infusion in Vial 25mg/mL (100mg/4 mL) (rDNA origin)</td></tr>
<tr><td>Therapeutic class</td><td>Monoclonal Antibodies</td></tr>
<tr><td>Dosage form:</td><td>Concentrate for solution for Infusion in Vial</td></tr>
<tr><td>Composition:</td><td>
<table>
<tr><th>Name of Ingredients</th><th>Concentration (mg/mL)</th><th>Strength (100mg/4mL)</th></tr>
<tr><td>Pembrolizumab (r-DNA Origin) In-house</td><td>25</td><td>100</td></tr>
<tr><td>L-Histidine USP/EP</td><td>0.3</td><td>1.2</td></tr>
<tr><td>L-histidine monohydrochloride monohydrate EP</td><td>1.7</td><td>6.8</td></tr>
<tr><td>Polysorbate 80 I.P./USP/EP</td><td>0.2</td><td>0.8</td></tr>
<tr><td>Sucrose I.P./USP/EP</td><td>70</td><td>280</td></tr>
<tr><td>Water for Injection I.P./USP/EP</td><td>q.s to 1.0 mL</td><td>q.s to 4.0 mL</td></tr>
</table>
</td></tr>
<tr><td>Indications:</td><td>Indicated for the treatment of Non Small Cell Lung Cancer (NSCLC)</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.	HCG City Cancer Centre, 33-25-33, Ch Venkata Krishnayya Street, Suryaraopet, Vijayawada-520002, Andhra Pradesh	Institutional Ethics Committee, HCG Curie City Cancer Centre, 44-1-1/3 padavalarevu, Gunadala Vijayawada Krishna, Andhra Pradesh-520004 EC reg no. ECR/869/Inst/AP/2016-RR-19	Dr. K. Lakshmi Priyadarshini
2.	IGIMS, Patna, State Cancer Institute, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna-800014, Bihar, India	Institutional Ethics Committee, IGIMS, Sheikhpura, Raja Bazar Patna, Bihar -800014 India EC Reg no. ECR/640/Inst/BR/2014/RR-20	Dr. Alok Ranjan
3.	Department of Medical Oncology, Cancer Block, Government Royapettah Hospital, Royapettah, Chennai-600014, Tamil Nadu	IEC GKMC Govt. Kilpauk Medical College and Hospital, The Dean GKMC, Chennai, Tamilanadu-600010 EC Reg no. ECR/1385/Inst/TN/2020	Dr. G. Raja

4.	MNJ Institute of Oncology & Regional Cancer Centre, Red Hills, Hyderabad-500004, Telangana,	MNJ Institute of Oncology & Regional Cancer Centre Ethics Committee, MNJ Institute of Oncology & Regional Cancer Centre, Red Hills, Hyderabad - 500004, Telangana EC reg no. ECR/227/Inst/AP/2013/RR-19	Dr. P. Radhika
5.	Rajiv Gandhi General Government Hospital, Madras, Park Town, Chennai Central, Chennai, Tamil Nadu- 600003	Institutional Ethics Committee The Voluntary Health Services Multi Specialty Hospital and Research Centre Rajiv Gandhi Salai, Adayyar, Chennai, Tamil Nadu – 600113 EC reg no. ECR/270/Inst/TN/2013/RR-20	Dr. Kannan Jayaraman
6.	Vardhman Mahavir Medical College and Safdarjung Hospital, Room No.701, 7th floor old SIC, Medical oncology Block, Vardhman Mahavir Medical College and Safdarjung Hospital New Delhi-110029	Institutional Ethics Committee VMMC and SJH VMMC and SAFDARJUNG HOSPITAL, Ring Road Ansari Nagar South Delhi, New Delhi - 110029 EC reg no. ECR/593/Inst/DL/2014/RR-20	Dr. Kaushal Kalra
7.	Sparsh Hospital, Bhubaneswar, A/407, Shaheed nagar, Bhubaneswar, Odisha, 751007	Institutional Ethics CommitteeSparsh Hospitals and Critical Care Private Limited Plot No-A/407, Saheed Nagar, Bhubaneswar Khordha, Odisha - 751007 EC Reg no. ECR/68/Inst/OR/2013/RR-22	Dr. Ghanashyam Biswas
8.	Tamil Nadu Government Multi Super Speciality Hospital, Omandurar Estate, Chennai-600002, Tamilnadu	Tamil Nadu Govt. Multi Super Specialty Hospital, Omandurar, Govt Estate, Anna Salai, Chennai, Tamil Nadu EC Reg no. ECR/1375/Inst/TN/2020	Dr. Prem Kumar Devdoss
9.	Unique Hospital Multispeciality & Research Institute, Opp. Kiran Motors, nr. Canal, Civil char rasta, sosyo circle lane , off. Ring road, Surat - 395002, Gujarat	Ethics committee, Unique Hospital Opp. kiran motors, nr. canal, civil char rasta sosyo circle lane, off. ring road, Surat, Gujarat EC reg no. ECR/595/Inst/GJ/2014/RR-20	Dr. Ankit Patel

10.	Basavatarakam Indo-American Cancer Hospital and Research Institute, Room No:367, 3rd Floor, Road No-10 Banjara hills, Hyderabad-500034, Telangana,	Institutional Ethics Committee, Basavatarakam Indo-American Cancer Hospital and Research Institute, Room No:367, 3rd Floor, Road No-10, Banjara Hills, Hyderabad-500034, Telangana EC reg no. ECR/7/Inst/AP/2013/RR-20	Dr. MVT Krishna Mohan
11.	Chittaranjan National Cancer Institute37 S.P. Mukheriee Road, Kolkata-700026, West Bengal	Institutional Ethics Committee Chittaranjan National Cancer Institute 37, S.P. Mukherjee Road, Kolkata 700026, West Bengal EC Reg no. ECR/241/Inst/WB/2013/RR-20	Dr. Kalyan Kusum Mukherjee
12.	LMMF'S, Deenanath Mangeshkar Hospital and Research centre, Erandawane, Pune 411004, Maharashtra	Institutional Ethics committee Deenanath Mangeshkar Hospital and Research Centre, Off Karve Road, Erandawane, Pune, Maharashtra EC reg no. ECR/15/Inst/Maha/2013/R-22	Dr. Sachin Sharadchandra Hingmire
13.	All India Institute of Medical Sciences, Ansari Nagar, New Delhi, 110029	Institute of ethics Committee AIIMS OT Block, Ansari Nagar, New Delhi-29 EC reg no. ECR/538/Inst/DL/2014/RR-20	Dr. Sachin Khurana