



Government of India
Central Drugs Standard Control Organisation (Headquarter)
(Directorate General of Health Services)
FDA Bhavan, ITO, Kotla Road
New Delhi - 110002 (Delhi)
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File No. BIO/CT/23/000050

Dated: 31-08-2023

To,

M/s. Hetero Biopharma Limited,
H.No. 8-3-166/1 & 2, 105 to 108
1st Floor, G Block, East Wing, Challa Estates,
Erragadda, Hyderabad (India)-500018

Subject: Application for grant of permission to conduct Phase IIIb clinical trial entitled – " A Phase IIIb, Prospective, Multicenter, Parallel, Assessor Blinded Extension Study to Evaluate the long-term Efficacy, Immunogenicity, Safety of Subcutaneous Injection of Denosumab (Hetero) in patients with bone metastases from solid tumours" as per Protocol No. HCR/IIIb/DENOSOLEXT/01/2023 Version1.0 Dated 08.03.2023- regarding

Ref. No.: Your Application No. BIO/CT04/FF/2023/36803 dated 31.03.2023

Sir,

With reference to your application No.: BIO/CT04/FF/2023/36803 dated 31-MAR-2023, 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) 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.

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, H.No. 8- 3-166/1 & 2, 105 to 108, 1st Floor, G Block, East Wing, Challa Estates, Erragadda, Hyderabad (India)-500018, Telephone No.: 40-23810110 FAX: 40-23810110 E-Mail: VIJAYNAG.T@HETERODRUGS.COM to conduct Phase IIIb clinical trial entitled – " A Phase IIIb, Prospective, Multicenter, Parallel, Assessor Blinded Extension Study to Evaluate the long-term Efficacy, Immunogenicity, Safety of Subcutaneous Injection of Denosumab (Hetero) in patients with bone metastases from solid tumours" as per Protocol No. HCR/IIIb/DENOSOLEXT/01/2023 Version1.0 Dated 08.03.2023 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: 31-Aug-2023

Digitally signed by RAJEEV SINGH
RAGHUVANSHI
DN: cn=Rajeev Singh Raghuvanshi,
o=RAJEEV SINGH RAGHUVANSHI,
ou=RAJEEV SINGH RAGHUVANSHI,
email=rajeev@rajeevsinghraghuvanshi.com,
c=IN, o=RAJEEV SINGH RAGHUVANSHI,
ou=RAJEEV SINGH RAGHUVANSHI,
serialNumber=657F54FD9D4098D8FB03BC
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Digitally signed by RAJEEV SINGH
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Annexure:**Details of new drug or investigational new drug:**

Names of the new drug or investigational new drug:	Denosumab (120 mg/1.7 mL) solution for injection (r-DNA origin)													
Therapeutic class	Anticancer													
Dosage form:	Denosumab injection 1.7 mL single use vial													
Composition:	Each vial contains: <table><tr><th>Name of Ingredients</th><th>Quantity 120mg/1.7mL (70mg/1mL) in vial</th></tr><tr><td>Denosumab, In-house</td><td>120 mg</td></tr><tr><td>Acetic acid glacial</td><td>18mM</td></tr><tr><td>Sorbitol (w/v)</td><td>4.6%</td></tr><tr><td>Sodium hydroxide</td><td>For pH adjustment</td></tr><tr><td>Water for injection (IP/USP)</td><td>q.s. to 1.7 mL</td></tr></table> Note: pH: 5.2±0.5		Name of Ingredients	Quantity 120mg/1.7mL (70mg/1mL) in vial	Denosumab, In-house	120 mg	Acetic acid glacial	18mM	Sorbitol (w/v)	4.6%	Sodium hydroxide	For pH adjustment	Water for injection (IP/USP)	q.s. to 1.7 mL
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Sodium hydroxide	For pH adjustment													
Water for injection (IP/USP)	q.s. to 1.7 mL													
Indications:	Prevention of skeletal related events in adults with advanced malignancies involving bone Treatment of adults and skeletally mature adolescents with giant cell tumour of bone													

Details of clinical trial site:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1.	MNJ Institute of Oncology & Regional Cancer Center Red hills, Hyderabad -500004	Institutional Ethics Committee MNJ Institute of Oncology & Regional Cancer Center Red hills, Hyderabad -500004 EC Reg. No.: ECR/227/Inst/AP/2013/RR-19	Dr. P. Radhika
2.	Department of Medical Oncology, Main OPD building 3rd floor, Room No. 313, Vardhman Mahavir Medical College & Safdarjung Hospital, Newdelhi - 110029	Institutional Ethics Committee Room No. 505 & 506, 5th floor, College Building, VMCC & Safdarjung Hospital, New Delhi-110029 EC Reg. No.: ECR/593/Inst/DL/2014/RR-20	Dr. Kaushal Kalra
3.	Indira Gandhi Institute of Medical Sciences, Regional Cancer Center, Sheikhpura, Patna - 800014, Bihar, India	Institutional Ethics Committee Indira Gandhi Institute of Medical Sciences, Regional Cancer Center, Sheikhpura, Patna - 800014, Bihar, India EC Reg. No.: ECR/640/Inst/BR/2014/RR-20	Dr. Rajesh Kumar Singh

4.	Institute of Post Graduate Medical Education & Research, 244 AJC Bose Road, Kolkata -700020, West Bengal, India	IPGME&R Research Oversight Committee, 244, AJC Bose Road, Kolkata -700020, West Bengal, India EC Reg. No.: ECR/35/Inst/WB/2013/RR-19	Dr. Koushik Chatterjee
5.	Department of Surgical Oncology, 3rd Floor, Shatabdi Phase 2, King George's Medical University, Chowk, Lucknow - 226003, Uttar Pradesh, India	Institutional Ethics Committee Office of the Research Cell, King George's Medical University, Chowk, Lucknow - 226003, Uttar Pradesh, India EC Reg. No. ECR/262/Inst/UP/2013/RR-19	Dr. Vijay Kumar
6.	Department of Radiation Oncology Room no.46, Fourth floor Dhanvantri OPD block, SMS Hospital, Jaipur-302004, Rajasthan, India	Ethics Committee SMS Medical College & Attached Hospitals, J L N Marg, Jaipur-302004, Rajasthan, India EC Reg No. ECR/26/Inst/RJ/2013/RR-19	Dr. Ravinder Singh Gothwal
7.	Basavatarakam Indo American Cancer Hospital & Research Institute, Road no - 10, Banjara hills, Hyderabad - 500034, Telangana, India	Institutional Ethics Committee Basavatarakam Indo American Cancer Hospital & Research Institute, Road no - 10, Banjara hills, Hyderabad -500034, Telangana, India EC Reg No. ECR/7/Inst/AP/2013/RR-20	Dr. MVT.Krishna Mohan
8.	SRM Medical College Hospital & Research Centre, Kattankulathur- 603203, Chengalpattu, Tamil Nadu, India	IEC, SRM Medical College Hospital & Research Centre, Kattankulathur-603203, Chengalpattu, Tamil Nadu, India EC Reg No. ECR/431/Inst/TN/2013/RR-19	Dr. V.M Durai Mavalavan
9.	Mumbai Oncocare Center(A unit of Cellcure Cancer Centre Pvt Ltd), 2nd floor, Majithia Apartments, S V Road, Vile Parle Mumbai-400056	Mumbai Oncocare Centre Institutional Ethics Committee(MOC-IEC), 1to 4, 1st floor, Shreepati Arcade, August Kranti Marg, Nana Chowk, Mumbai -400036, Maharashtra EC Reg No. ECR/1277/Inst/MH/2019	Dr. Kshitij Chandrakant Joshi
10.	Netaji Subhash Chandra Bose Cancer Hospital, 3081 Nayabad, NewGaria, Kolkata- 700094, West Bengal, India	Ethics Committee, N.S.C.B.C Research Institute (Netaji Subhash Chandra Bose Cancer Hospital) 3081 Nayabad, New Garia, Kolkata- 700094, West Bengal, India EC Reg No. ECR/286/Inst/WB/2013/RR-19	Dr. Anupam Datta

11.	Unique Hospital Multispeciality and Research Institute, Opp. Kiran Motors, Near Canal, Civil Char Rasta, Sosyo Circle Lane, Off Ring Road, Surat - 395002, Gujarat, India	Ethics Committee, Unique Hospital Multispeciality and Research Institute, Opp. Kiran Motors, Near Canal, Civil Char Rasta, Sosyo Circle Lane, Off Ring Road, Surat - 395002, Gujarat, India EC Reg No. ECR/595/Inst/GJ/2014/RR-20	Dr. Ankit Patel
12.	HCG Cancer Centre, 33-22- 33,Ch Venkata krishnayya, street, Suryarao pet, Vijayawada 520002, Andhra Pradesh, India	Institutional Ethics Committee, HCG Curie City Cancer Centre, 44-1-1/3, Padavalarevu, Gundala, Vijayawada 520004, Andhra Pradesh, India EC Reg No. ECR/869/Inst/AP/2016/RR-19	Dr. K. L. Priyadarshini
13.	Kamalnayan Bajaj Hospital, Gut No. 43, Satara Parisar, Beed Bypass Road, Aurangabad-431010, Maharashtra, India	Ethics Committee, Kamalnayan Bajaj Hospital, Gut No. 43, Satara Parisar, Beed Bypass Road, Aurangabad-431010, Maharashtra, India EC Reg No. ECR/444/Inst/MH/2013/RR-20	Dr. Zawar Abhinav Bhagwan