

File No: BIO/CT/23/000088
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(Biological Division)

From:

The Drugs Controller General, India
Directorate General of Health Services,

FDA Bhawan, Kotla Road,
New Delhi-110002
Dated: 29.01.2024

To,

M/s Lupin Limited, Biotechnology Division,
Gat No. 1156, 1157, 1158, 1159 and 1160,
Village Ghotawade, Taluka Mulshi,
Pune, Maharashtra (India) – 412115

Subject: Application for grant of permission to conduct pharmacokinetic study titled – “A double blind, randomized, single-period, two-treatment, parallel, balanced, single dose study to compare pharmacokinetic, pharmacodynamic and immunogenicity of Denosumab 60 mg prefilled syringe solution for injection (60 mg/mL) and Prolia® (Denosumab) 60 mg solution for injection (60 mg/mL) in pre-filled syringe in healthy adult male subjects” vide protocol no. C1B03215, version 2.0 dated 11.12.2023 - regarding

Ref.: Your Application No. BIO/CT04/FF/2023/37174 dated 30-06-2023

Sir,

With reference to your Application No.: BIO/CT04/FF/2023/37174 dated 30-06-2023, 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:
- (III) 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;
- (IV) 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;
- (V) 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;

- (VI) 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;
- (VII) 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;
- (VIII) 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;
- (IX) 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;
- (X) 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;
- (XI) 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;
- (XII) 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;
- (XIII) 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;
- (XIV) 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;
- (XV) 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;
- (XVI) The laboratory owned by any person or a company or any other legal entity and utilized 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;
- (XVII) 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;

- (XVIII) The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.
- (XIX) 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.
- (XX) The firm shall submit clinical study report to this office after completion of the study.

RAJEEV SINGH
RAGHUVANSHI
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Yours faithfully,

Digital Signature of RAJEEV SINGH RAGHUVANSHI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL
ORGANIZATION, ou=RAJEEV SINGH RAGHUVANSHI,
2.5.4.20=80c62f6a23e4eafbe8a239774cdeb03c276904
1015a06564fe67f54b765db1cb, postalCode=600034,
st=TAMIL NADU,
serialNumber=657F5E47D940985D8F038DC902D0E1F
E73CFA12A1A126EA94FA5701124A19013, cn=RAJEEV
SINGH RAGHUVANSHI
Date: 2024.01.29 15:59:52 +05'30'

(Dr. Rajeev Singh Raghuvanshi)
Central 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 Licencing Authority hereby permits **M/s Lupin Limited, Biotechnology Division, Gat No. 1156, 1157, 1158, 1159 and 1160, Village Ghotawade, Taluka Mulshi, Pune, Maharashtra (India) – 412115**, to conduct clinical trial of the new drug or investigational new drug study titled “A double blind, randomized, single-period, two-treatment, parallel, balanced, single dose study to compare pharmacokinetic, pharmacodynamic and immunogenicity of Denosumab 60 mg prefilled syringe solution for injection (60 mg/mL) and Prolia® (Denosumab) 60 mg solution for injection (60 mg/mL) in pre-filled syringe in healthy adult male subjects” vide protocol no. C1B03215, version 2.0 dated 11.12.2023 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.

Place: New Delhi

Date: 29.01.2024

**RAJEEV SINGH
RAGHUVANSHI**

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

Digitally signed by RAJEEV SINGH RAGHUVANSHI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL
ORGANIZATION, ou=RAJEEV SINGH RAGHUVANSHI,
2.5.4.20=80c626a23e4e4b8a239774cde803c2769041015a
0c544e67f54b765db1cb, postalCode=600034, st=TAMIL
NADU,
serialNumber=657F5E47D940985D8F03BDC902D0E1FE73C
FA12A1A126EA94FA5701124A19013, cn=RAJEEV SINGH
RAGHUVANSHI
Date: 2024.01.29 16:00:27 +05'30'

Annexure:**Details of new drug or investigational new drug:**

Names of the new drug or investigational new drug	Lupin Denosumab (r-DNA origin) solution for injection 60 mg/ml		
Therapeutic class	Antiresorptive		
Dosage form:	Solution for injection presented in 1 mL single-dose prefilled syringe (PFS) for subcutaneous administration.		
Composition:	Name of Ingredient	Lupin Denosumab Qty. per PFS	Ref. Denosumab (Prolia) Qty. per PFS
	Denosumab IH	60 mg	60 mg
	Sorbitol USP	6.19 mg	4.7%
	Glacial acetic acid (0.2M) USP	18mM	17mM
	Polysorbate 20 USP	0.01%	0.01%
	Sodium hydroxide USNF (1M)	q.s. to pH 5.2	q.s. to pH 5.2
	Water for injection USP	q.s. to 1 ml	q.s. to 1 ml
Indications:	Denosumab is indicated for the treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures.		

Details of clinical trial site:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1	Cliantha Research Limited Dream Arcadia, Opp. Mayfair Atrium, Vadsar-Kalali Ring Road Vadodara – 390012 Gujarat, India	Anand Institutional Ethics Committee Anand Multispeciality Hospital B Tower Sundarvan Complex Beside IOCL Petrol Pump Near Gorwa ITI, Vadodara – 390016, Gujarat, India. <u>EC Reg. No.</u> <u>ECR/725/Inst/GJ/2015/RR-21</u>	Dr. Dharit Shah