



File No. BIO/CT/23/000009

Dated 28-Apr-2023

To,

M/s. Enzene Biosciences Ltd.,  
Plot No. A 22, A1/2, Chakan Industrial Area,  
Phase 2, Khalumbre Chakan, Pune-410501

Subject: Application for grant of permission to conduct Phase IV clinical trial entitled – "A prospective, multicenter, Open labelled, Phase IV study to evaluate safety & Efficacy of Biosimilar Adalimumab injection of Enzene Biosciences Ltd. in subjects with active Ankylosing spondylitis (AS)." as per Protocol No.: ALK29/ENZ129-ADA2 Version:1.0, Date: 15.01.2023- regarding

Ref. No.: Your Application No. BIO/CT04/FF/2023/35806 dated 27.01.2023

Sir,

With reference to your application No.: BIO/CT04/FF/2023/35806 dated 27JAN-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) Firm shall exclude latent TB patients from the study as recommended by Subject Expert Committee in its 94<sup>th</sup> meeting held on 15.03.2023 and accordingly submit revised protocol to this Directorate before initiation of study.**
- (II) 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
- (III) 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;
- (IV) 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;
- (V) 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;
- (VI) 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.

- (VII) 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.
- (VIII) 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;
- (IX) 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.
- (X) 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.
- (XI) 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.
- (XII) 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.
- (XIII) 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.
- (XIV) 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.
- (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 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.
- (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 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.

## 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. Enzene Biosciences Ltd., Plot No. A 22, A1/2, Chakan Industrial Area, Phase 2, Khalumbre Chakan, Pune-410501 (India), Telephone No.: 02135614300 FAX: 2030674620 E-Mail : HARISH.SHANDILYA@ENZENE.COM to conduct Phase IV clinical trial entitled – **"A prospective, multicenter, Open labelled, Phase IV study to evaluate safety & Efficacy of Biosimilar Adalimumab injection of Enzene Biosciences Ltd. in subjects with active Ankylosing spondylitis (AS)"** as per Protocol No.: ALK29/ENZ129-ADA2; Version:1.0, Date: 15.01.2023 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. **Firm shall exclude latent TB patients from the study as recommended by Subject Expert Committee in its 94th meeting held on 15.03.2023 and accordingly submit revised protocol to this Directorate before initiation of study.**
5. 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: 28-Apr-2023

RAJEEV SINGH  
(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,  
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041015a06564f667b540765db1cd,  
postalCode=500034, st=TELANGANA, serialNumber=657F5E47D940985D8F038D0C202D0E  
Date: 2023.05.01 12:45:22 +05'30'

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

Names of the new drug or investigational new drug:	Adalimumab Injection 20mg/0.2mL, 40mg/0.4mL, 80mg/0.8mL (r-DNA origin)			
Dosage form:	Solution for injection in Pre filled syringe			
Composition:	Each vial contains:			
	<b>Name of Ingredients</b>	<b>For 20mg/0.2mL</b>	<b>For 40mg/0.4mL</b>	<b>For 80mg/0.8mL</b>
	Adalimumab Drug Substance (in house)	20 mg	40 mg	80 mg
	Mannitol (IP)	8.4 mg	16.8 mg	33.6 mg
	Polysorbate 80 (IP)	0.2 mg	0.4 mg	0.8 mg
	Water for injection (IP)	q.s. to 0.2mL	q.s. to 0.4mL	q.s. to 0.8mL
Indications:	Treatment of patients with Active Ankylosing Spondylitis			

**Details of clinical trial site:**

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1.	Medipoint Hospitals Pvt. Ltd., 241/1 New D.P road, Aundh, Pune 411007, Maharashtra, India	Penta-Med Ethics Committee Medipoint Hospitals Pvt. LtdsMedipoint Hospitals Pvt. Ltd 241/1, New D.P.Road, Near Sai Heritage, Aundh. Pune Maharashtra -411007 India EC Reg. No.: ECR/357/Inst/MH/2013/RR-20	Dr. Girish Gokuldas Bhatia
2.	Department of Orthopedics, Queen's NRI Hospital, Gurudwara Lane, Seethammadara, Visakhapatnam-530013, Andhra Pradesh, India	Institutional Ethics Committee, Queens NRI Hospital Seethammadhara, Gurudwara Lane, Vishakhapatnam Visakhapatnam Andhra Pradesh -530013 India EC Reg. No.: ECR/145/Inst/AP/2013/RR-20	Dr. Karumunchi Vasantha Babu
3.	All India Institute of Medical Services, Room No. 4076, 4thFloor, Teaching Block, AIIMS, New Delhi	Institutional Ethics Committee All India Institute of Medical Services, Old OT Block, Room No. 102, AIIMS Hospital Ansari Nagar, South Delhi, Delhi, 110029, India EC Reg. No.: ECR/538/Inst/DL/2014/RR-20	Dr. Uma Kumar

4.	Sushruta multispecialty Hospital & research Center Pvt. Ltd., P.B. Road, Vidhyanagar, Hubballi-580021, Karnataka, India	Sushruta Hospital Ethics CommitteeC/o Sushruta multispecialty Hospital & research Center Pvt. Ltd., P.B. Road, Vidhyanagar, Hubballi-580021, Karnataka, India  ECR/372/Inst/KA/2013/RR-19	Dr. Vikram Muralidar Haridas
5.	Sangini Hospital, 401-402, 4 <sup>th</sup> Floor, Santorini Square, Opp Star Bazar, Behind Abhishree Complex, Nr Satellite Road, Ahmedabad 380015	Sangini Hospital Ethics Committee, Sangini Hospital Santorini Square, B/H Abhishree Complex, Opp. Star Bazar, Nr Jodhpur Cross Roads, Satellite Ahmedabad, Gujarat-380015  EC Reg. No. ECR/147/Inst/GJ/2013/RR-19	Dr. Vishnu Sharma