



File No. BIO/CT/23/000096

Dated 10-Sep-2024

To,
M/s Sandoz Private Limited,
MIDC, Plot Nos. 8-A/2 & 8-B,
TTC Industrial Area, Kalwe Block,
Village Dighe, Navi Mumbai, Maharashtra -400708 (India)

Subject: Application for grant of permission to conduct Phase IV clinical trial entitled "A prospective, multi-center, open-label, phase IV study to evaluate the safety and effectiveness of intravitreal injections (IVI) of Brolocizumab in patients with Diabetic Macular Edema (DME)" vide protocol CRTH258BIN01 version 01 dated 22.05.2024- regarding

Ref.:Your Application No BIO/CT04/FF/2023/38544 dated 14-Jul-2023

Sir,

With reference to your Application No BIO/CT04/FF/2023/38544 dated 14-Jul-2023, 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) The firm should submit details of clinical trial sites after obtaining approval of Ethics committee for conducting clinical trial to CDSCO.
- (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 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;
- (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) The permission to initiate clinical trial granted under rule 22 in form CT-06 or automatic approval under rule 23 in Form CT 4A shall remain valid for a period of two years from the date of its issue, unless extended by the Central Licensing Authority.
- (XIX) The firm should submit Clinical study report (CSR) to this office after completion of trial.

RAJEEV SINGH
RAGHUVANSHI

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(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

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 Sandoz Private Limited, MIDC, Plot Nos. 8-A/2 & 8-B, TTC Industrial Area, Kalwe Block, Village Dighe, Navi Mumbai, Maharashtra -400708 (India) to conduct clinical trial of the new drug or investigational new drug Phase IV study titled entitled "A prospective, multi-center, open-label, phase IV study to evaluate the safety and effectiveness of intravitreal injections (IVI) of Brolucizumab in patients with Diabetic Macular Edema (DME)" vide protocol CRTH258BIN01 version 01 dated 22.05.2024 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.

Place: New Delhi
Date: 10-Sep-2024

**RAJEEV SINGH
RAGHUVANSHI**

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

CDSCO

CDSCO

MINISTRY OF HEALTH, GOVERNMENT OF INDIA
सत्यमेव जयते

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

Name of the new drug	Brolucizumab solution for injection 120 mg/mL (r-DNA origin)		
Dosage form	Solution for Injection (1 Vial + 1 filter needle)		
Composition	Each mL of Brolucizumab solution for injection contains –		
	Name of Ingredients	Concentration (mg/mL)	Function
	Brolucizumab (In-house Specification)	120 mg	Active
	Sucrose (Ph.Eur,USP/NF)	58 mg	Stabilizer and tonicity agent
	Sodium citrate (Ph. Eur; USP/NF)	2.58 mg	Buffering agent
	Polysorbate 80 (Ph. Eur; USP/NF)	0.20 mg	Stabilizer and surfactant
	Sodium hydroxide (Ph. Eur; USP/NF)	pH 7.2	pH adjusting agent
	Nitrogen (Ph. Eur; USP/NF)	q.s.	Processing aid
	Water for injections (Ph. Eur; USP/NF)	ad 1 mL, 1059 mg	Solvent
Indications	For the treatment of DME(Diabetic Macular Edema)		