

F. No. BIO/CT/20/000037
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

To,

M/s Biocon Biologics India Limited,
Biocon House, Semicon Park,
Electronics City, Phase –II,
Bengaluru –560 100, India

Subject: Application for grant of permission to conduct Phase II clinical trial entitled “A Multi-Centric, Open label, Two Arm Randomized, Pivotal Phase - II Trial to Study the Efficacy and Safety of Itolizumab in COVID-19 Complications”, vide Protocol No.: ITOLI-C19-02-I-00, Version No.: 03 Dated: 09.04.2020 – regarding

Sir,

With reference to your application No. BIO/CT04/FF/2020/19216, dated 02.04.2020, please find enclosed herewith the permission in FORM CT-06 for conduct of subject mentioned pivotal Phase II 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;
- vii. 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;
- viii. 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;
- ix. 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;
- x. 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;
- xi. 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;
- xii. 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;
- xiii. 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;

- xiv. Where the new drug or investigational new drug is found to be useful in clinical development, the sponsor shall submit an application to the Central Licensing Authority for permission to import or manufacture for sale or for distribution of new drug in India, in accordance with Chapter X of these rules, unless otherwise justified;
- 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. Submit of copy of the Insurance Certificate, investigator's undertaking as per Table 4 of Third Schedule of NDCT Rules 2019 along with Medical registration certificate for the investigator's mentioned by you in FORM CT-04 before initiating the trial.
- xix. Additional 5-7 study/by sites should be included in the study and the same should be intimated to this office before initiating the trial.
- xx. The cut-off limits should be specified for all biomarkers for inclusion of the subject in the study. In addition to cytokine, Th 17, T-effector cells should be assessed. The revised protocol should be submitted to CDSCO before initiation of the study.

Yours faithfully

VENUGOPAL
GIRDHARILAL
SOMANI

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(Dr. V. G. Somani)

Drugs Controller General (India)
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 M/s Biocon Biologics India Limited, Biocon House, Semicon Park, Electronics City, Phase –II, Bengaluru –560 100, India to conduct clinical trial of the new drug or investigational new drug as per Protocol No: ITOLI-C19-02-I-00; Version 03, Dated: 09.04.2020 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:09-Apr-2020

VENUGOPAL
GIRDHARILAL
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(Dr. V. G. Somani)

Drugs Controller General (India)
Central Licencing Authority

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

Names of the new drug or investigational new drug	Itolizumab Injection (r-DNA origin, Itolizumab is a humanized recombinant anti-CD6 monoclonal antibody) 25 mg/5 mL solution for intravenous infusion in vials.			
Therapeutic class	Immunomodulator			
Dosage form:	Parenteral (Solution for intravenous infusion only). Single use vial. Each single use 5 mL vial contains Itolizumab (rDNA Origin) 25 mg.			
Composition:	Sr.No.	Name of Ingredient	Amount per Vial	Referenced monograph
	1	Itolizumab (rDNA Origin) MAb (Active substance)	25.0 mg	In-house
	2	Monobasic Sodium Phosphate (Buffer)	3.0 mg	IP
	3	Dibasic Sodium Phosphate (Buffer)	9.0 mg	EP

	4	Sodium Chloride (Buffer)	44.0 mg	IP
	5	Polysorbate 80 (surfactant)	1.0 mg	IP
	6	Water for Injection q.s.	qs to 5 mL	IP
Indications:		COVID 19 Complication (Cytokine Release Syndrome)		

Details of clinical trial site:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1.	NH Mazumdar Shaw Medical Centre 258/A, Bommasandra Industrial Estate, Anekal Taluk, Bangalore- 560099	The Chairman Narayana Health Medical Ethics Committee, Narayana Health, Hospital Health City, No. 258/A, Bommasandra Industrial Area Anekal Taluk Bengaluru Rural -560099, Karnataka, India. <u>EC Reg. No.</u> <u>ECR/390/Inst/KA/2013/RR-19</u>	Dr. Murali Mohan Bangalore Venkataraman
2.	KEM Hospital and Research Centre., Sardar Moodliar Road, Pune – 411011, Maharashtra, India	KEM Hospital Research Centre Ethics Committee KEM Hospital Ressearch centre TDH Building Rasta Peth III rd Floor, 303, Pune Maharashtra – 411011, India. <u>EC Reg. No.</u> <u>ECR/272/Inst/MH/2013/RR19</u>	Dr. Pradeep Dcosta