

File No: BIO/CT/20/000003
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 Cipla Limited, Cipla House,
Peninsula Business Park Ganpatrao Kadam Marg,
Lower Parel, Mumbai Lower Parel (India) - 400013

Subject: Application for grant of permission to conduct clinical trial entitled – “Phase IV, open label, non-comparative, multicentre study to evaluate safety and efficacy of subcutaneous Tocilizumab in subjects with giant cell arteritis (GCA)” vide Protocol Study Code: CP/07/19, Version 02, dated 15.04.2020 - regarding

Ref.: Your Application No. BIO/CT04/FF/2020/18184 dated 16-Jan-2020

Sir,

With reference to your Application No.: BIO/CT04/FF/2020/18184 dated 16-Jan-2020, 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) 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 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;
- (XIV) 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;
- (XV) 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;
- (XVI) The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.
- (XVII) You should include more government sites for the subject study.**

Yours faithfully,


Digitally signed by VENUGOPAL
GIRDHARILAL SOMANI
DN: c=IN, o=MINISTRY OF HOME AFFAIRS,
ou=CDSCO DGHS, postalCode=431401,
*cn=VenuGopal
2.5.4.20=773083345802489623799147
1840498220a5648380a315409991a
f7, cn=VENUGOPAL GIRDHARILAL SOMANI
Date: 2020.07.03 16:18:13 +05'30'

(Dr. V. G. Somani)
Central Licensing Authority

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

Names of the new drug or investigational new drug:	Tocilizumab Injection [180mg/mL Prefilled Syringes (162mg/0.9mL)]																																			
Therapeutic class:	Recombinant humanized antihuman IL-6 receptor																																			
Dosage form:	Single use prefilled syringe (PFS) for subcutaneous (SC) injection, delivering 162 mg Tocilizumab in a 0.9 mL solution																																			
Composition:	<table border="1"> <thead> <tr> <th>Name of Ingredient</th> <th>Concentration</th> <th>Function</th> <th>Specifications</th> </tr> </thead> <tbody> <tr> <td>Tocilizumab</td> <td>180 mg/ml</td> <td>Active</td> <td>In House</td> </tr> <tr> <td>L-Histidine HCl Monohydrate</td> <td>20 mM</td> <td>Inactive</td> <td>U.S.P.,E.P.,J.P.</td> </tr> <tr> <td>L-Histidine</td> <td>20 mM</td> <td>Inactive</td> <td>U.S.P.,E.P.,J.P.</td> </tr> <tr> <td>L-Methionine</td> <td>30 mM</td> <td>Inactive</td> <td>U.S.P.,E.P.,J.P.</td> </tr> <tr> <td>L-Arginine Hydrochloride</td> <td>100 mM</td> <td>Inactive</td> <td>U.S.P.,E.P.,J.P.</td> </tr> <tr> <td>L-Arginine</td> <td>100 mM</td> <td>Inactive</td> <td>U.S.P.,E.P.,J.P.</td> </tr> <tr> <td>Polysorbate 80</td> <td>0.02 % w/v</td> <td>Inactive</td> <td>U.S.P.,E.P.,J.P.</td> </tr> </tbody> </table>				Name of Ingredient	Concentration	Function	Specifications	Tocilizumab	180 mg/ml	Active	In House	L-Histidine HCl Monohydrate	20 mM	Inactive	U.S.P.,E.P.,J.P.	L-Histidine	20 mM	Inactive	U.S.P.,E.P.,J.P.	L-Methionine	30 mM	Inactive	U.S.P.,E.P.,J.P.	L-Arginine Hydrochloride	100 mM	Inactive	U.S.P.,E.P.,J.P.	L-Arginine	100 mM	Inactive	U.S.P.,E.P.,J.P.	Polysorbate 80	0.02 % w/v	Inactive	U.S.P.,E.P.,J.P.
	Name of Ingredient	Concentration	Function	Specifications																																
	Tocilizumab	180 mg/ml	Active	In House																																
	L-Histidine HCl Monohydrate	20 mM	Inactive	U.S.P.,E.P.,J.P.																																
	L-Histidine	20 mM	Inactive	U.S.P.,E.P.,J.P.																																
	L-Methionine	30 mM	Inactive	U.S.P.,E.P.,J.P.																																
	L-Arginine Hydrochloride	100 mM	Inactive	U.S.P.,E.P.,J.P.																																
	L-Arginine	100 mM	Inactive	U.S.P.,E.P.,J.P.																																
Polysorbate 80	0.02 % w/v	Inactive	U.S.P.,E.P.,J.P.																																	
Indications:	<p>Indicated in combination with tapering glucocorticoid therapy for the treatment of giant cell arteritis in adult patients requiring no more than 60mg prednisone per day (or an equivalent drug) at initiation of Tocilizumab with regimen as follows-</p> <ol style="list-style-type: none"> 1. Dosage in patients with new-onset GCA: 162mg s.c. every two weeks, combined with a tapering course of glucocorticoids. 2. Dosage in patients with relapsing GCA: 162mg s.c. once weekly, combined with a tapering course of glucocorticoids. 																																			

Details of clinical trial sites:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1	AIIMS, Department of Rheumatology, Room No. 4076, 4077, Fourth Floor, Teaching Block, Ansari Nagar, New Delhi-110029, India	Ethics Committee, AIIMS, Room No. 102 1st Floor Old, O.T Block, Ansari Nagar New Delhi -110029 EC Reg. No.: ECR/538/Inst/DL/2014/RR-17	Dr. Danveer Bhadu
2	SRMC, Sri Ramachandra Institute of Higher Education and Research, No-1, Ramachandra Nagar, Porur, Chennai - 500116, Tamil Nadu, India	Institutional Ethics Committee, SRIHER, 1, Ramachandra Nagar, Porur, Chennai, Tiruvallur, Tamil Nadu - 600116 EC Reg. No.: ECR/203/Inst/TN/2013/RR-19	Dr. S. Rajeshwari
3	Apollo Gleneagles Hospital 58, Canal Circular Road Kolkata – 700054, West Bengal, India	Institutional Ethics Committee, Apollo Gleneagles Hospital 58, Canal Circular Road, Kolkata -700054, West Bengal EC Reg. No.: ECR/373/Inst/WB/2013/RR-19	Dr. Syamasis Bandopadhyay
4	CIMS, Care Institute of Medical Science Off Science City Road, Sola, Ahmedabad - 380060, Gujarat, India	Ethics Committee of Care Institute of Medical Science, Off Science City Road, Sola, Ahmedabad - 380060, Gujarat, EC Reg. No.: ECR/206/Inst/GJ/2013/RR-16	Dr. Reena Sharma