

F. No. BIO/CT/19/000030
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 Pfizer Products India Private Limited,
The Capital, 1802/1901, Plot No. C-70, G Block,
Bandra Kurla Complex, Bandra (East),
Mumbai-400051, Maharashtra, India

Subject: Application for grant of permission to conduct Phase IV clinical trial entitled "A single country, multicenter, open-label and non-randomized clinical trial with MOROCTOCOG ALFA (AFCC) prophylaxis and treatment of bleeding episodes in previously treated patients with moderate and severe Haemophilia A for a duration of 8 weeks", Protocol Number: B1831097, Amendment 1, dated 16 September 2019 – regarding

Sir,

With reference to your application No. BIO/Form44/FF/2019/14022, dated 30.04.2019, please find enclosed herewith the permission in FORM CT-06 for conduct of subject mentioned 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 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.

Yours faithfully

(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 Licensing Authority hereby permits **M/s Pfizer Products India Private Limited, The Capital, 1802/1901, Plot No. C-70, G Block, Bandra Kurla Complex, Bandra (East), Mumbai-400051, Maharashtra, India** to conduct Phase IV clinical trial of the new drug as per Protocol Number: B1831097, Amendment 1, dated 16 September 2019 in the below mentioned clinical trial sites [as per Annexure].

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:

(Dr. V. G. Somani)
Drugs Controller General (India)
Central Licensing Authority

Annexure:

Names of the new drug or investigational new drug:	Moroctocog Alfa (AF-CC) lyophilized powder for reconstitution														
Therapeutic class:	Antihemorrhagics; Blood Coagulation Factor VIII														
Dosage form:	Lyophilized powder for reconstitution														
Composition:	<p>Each vial contains:</p> <table border="1"> <thead> <tr> <th>Ingredients</th> <th>Quantity per vial</th> </tr> </thead> <tbody> <tr> <td>Moroctocog Alfa (AF-CC)</td> <td>250 IU or 500 IU or 1000 IU or 2000 IU</td> </tr> <tr> <td>L-Histidine (USP, Ph. Eur.)</td> <td>6 mg</td> </tr> <tr> <td>Sodium Chloride (USP, Ph. Eur.)</td> <td>36 mg</td> </tr> <tr> <td>Sucrose (NF, Ph. Eur.)</td> <td>12 mg</td> </tr> <tr> <td>Polysorbate 80 (NF, Ph. Eur.)</td> <td>0.4 mg</td> </tr> <tr> <td>Calcium Chloride Dihydrate (USP, Ph. Eur.)</td> <td>1.0 mg</td> </tr> </tbody> </table>	Ingredients	Quantity per vial	Moroctocog Alfa (AF-CC)	250 IU or 500 IU or 1000 IU or 2000 IU	L-Histidine (USP, Ph. Eur.)	6 mg	Sodium Chloride (USP, Ph. Eur.)	36 mg	Sucrose (NF, Ph. Eur.)	12 mg	Polysorbate 80 (NF, Ph. Eur.)	0.4 mg	Calcium Chloride Dihydrate (USP, Ph. Eur.)	1.0 mg
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Indications:	Moroctocog Alfa (AF-CC), Antihemophilic factor (recombinant) [BDDrFVIII] indicated for the control and prevention of hemorrhagic episodes and for routine and surgical prophylaxis in patients with haemophilia A (congenital factor VIII deficiency or classic hemophilia).														

Details of clinical trial sites:

S. No.	Names and address of clinical trial site	Ethics committee details	Name of principal investigator
1	Sahyadri Super Specialty Hospital, 30C, Erandwane, Karve Road, Pune-411004, Maharashtra, India	Sahyadri Hospitals Ltd Ethics Committee, Sahyadri Clinical Research and Development Center, 33/34b, Makarand Bhave Path, Karve Road, Pune – 411004, Maharashtra, India. EC Reg No.: ECR/493/Inst/MH/2013/RR-16	Dr Shashikant Janardan Apte
2	Nirmal Hospital Private Limited, Ring Road, Surat – 395002, Gujarat, India	Nirmal Hospital Private Limited Ethics Committee, Ring Road, Surat – 395002, Gujarat, India EC Reg No.: ECR/390/Inst/GJ/2013/RR-16	Dr Nirmalkumar Ganeshmal Choraria
3	Maulana Azad Medical College and Lok Nayak Hospital, Haemophilia Day Care Center, New Medicine Block, Bahadur Shah Zafar Marg, New Delhi-110002.	Institutional Ethics Committee, Maulana Azad Medical College, Bahadur Shah Zafar Marg, New Delhi-110002. EC Reg No.: ECR/329/Inst/DL/2013/RR-16	Dr Gupta Naresh Kumar