

MINUTES OF THE 21st MEETING OF THE APEX COMMITTEE HELD ON
27-02-2015 UNDER THE CHAIRMANSHIP OF SECRETARY, (HF&W) FOR
SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES

Present:

1. SHRI B.P. SHARMA
Secretary
Department of Health and Family Welfare
Ministry of health and Family Welfare &
Chairman, Apex Committee
2. DR. V.M. KATOCH
Secretary, DHR, & DG ICM
3. DR. JAGDISH PRASAD
DG, DGHS
4. SHRI K.L. SHARMA
Joint Secretary
Department of Health and Family Welfare

SPECIAL INVITEES:

1. SHRI N.S. KANG
Addl. Secretary & DG (CGHS)
Ministry of Health and Family Welfare
2. DR. G.N. SINGH
DCG(I), FDA Bhavan, New Delhi

Initiating the discussion, Chairman, Apex Committee welcomed the members of the Committee and special invitees to the meeting. Thereafter, the agenda items and recommendations of the 22nd Technical Committee were taken up for consideration. The decisions taken by the Apex Committee on each agenda items are as below:

1. Adoption of minutes of the 20th Meeting of the Apex Committee

The Apex Committee adopted the minutes of the 20th Apex Committee meeting held on 30.01.2015.

2. Proposals of Clinical Trials of NCEs recommended by Technical Committee

2.1 The Committee noted that the Technical Committee had evaluated 03 cases related to clinical trial of NCEs and made recommendations considering all aspects of safety, efficacy especially in terms of the three parameters viz. risk versus benefit to the patients, innovation vis-a-vis existing therapeutic option and unmet medical need in the country.

2.2 The Apex Committee deliberated upon the 03 cases of clinical trial proposals related to NCEs based on the direction of the Hon'ble Supreme Court order dated 03.01.2013. The Technical Committee had recommended these proposals at (Annexure-I).

Recommendation: After deliberations, the Apex Committee concurred with the recommendations of the Technical Committee.

3. Proposal of Clinical Trial Waiver in Indian population for approval of new drugs, which have already been approved outside India

3.1. As per the Drugs & Cosmetics Rules, for new drugs substances approved in other countries, phase III clinical trial is required before granting permission to manufacture / import of finished formulation of the new drug.

3.2. However, requirements of local Clinical Trial may be waived off / relaxed under certain conditions as per Drugs & Cosmetics Rules (122 A (2), 122 B (3) & clause 1 (3) of Schedule Y as mentioned above depending on the nature of drugs and diseases for which it is indicated.

3.3. Under Rule-122A(2) and Rule-122B(3) of Drugs & Cosmetics Rules the requirement of submitting the results of local clinical trials may not be necessary if the drug is of such a nature that the licensing authority may, in public interest, decide to grant such permission on the basis of data available from other countries. Further, the submission of requirements relating to animal toxicology data may also be modified or relaxed under the same Rules in case of new drugs approved and marketed for several years in other countries and adequate published evidence regarding the safety of the drug is available.

3.4. As per Clause 1 (3) of Schedule Y to Drugs & Cosmetics Rules, for drugs indicated in life threatening / serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority.

3.5. It would be thus observed that there are certain conditions specified in the Drugs & Cosmetics Rules under which the licensing authority may grant permission to manufacture / import of new drugs without local clinical trials.

3.6. However, Parliamentary Standing Committee in its 59th report expressed concerns on approval of certain new drugs in the country without local clinical trials. In this light, the Ministry constituted a Committee under chairmanship of Prof. Ranjit Roy Chaudhury, the Committee submitted its report. The action to be taken on the recommendations of the Expert Committee has been finalized by the Ministry of Health & Family Welfare.

3.7. Accordingly, "the waiver of Clinical Trial in Indian population for approval of new drugs, which have already been approved outside India, can be considered only in cases of national emergency, extreme urgency, epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy.

3.8. The Apex Committee in its meeting held on 24.01.2014 recommended that waiver of local clinical trial of such cases should be granted only under the criteria as already decided by the Ministry viz national emergency, extreme urgency, epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy. In case local clinical trial waiver is required for any other category, the matter should be brought before the Committee for consideration along with the recommendations of the Technical Committee.

3.9. Following 06 proposals (05 from New Drug and 01 from Medical device) have been recommended by the SECs for their approval for manufacture/ import for marketing in the country without local clinical trial. The details of the same along with recommendations of SEC were placed before the Committee for perusal and comments: The recommendations of the Technical Committee is as under.

Sr. no.	Drug Name	Name of the Firm	Indication	Recommendations
1. N.P	Pralatrexate Injection 20mg/mL & 40mg/2mL	M/s. Hetero Drugs Limited	For the treatment of patients with relapsed or refractory peripheral T-cell Lymphoma (PTCL).	<p>Recommendation: After detailed deliberation, the Technical Committee recommended the waiver of local clinical trial as per the recommendation of the SEC.</p> <p>SEC Recommendation: After detailed deliberation, the Committee observed that incidence of PTCL in the Country is very rare and is an Orphan disease. The Committee recommended that local clinical trial waiver may be granted for the said Indication with a condition that a PK study on 12 subjects should be conducted before issuing permission for marketing the drug in the country and a Phase IV post marketing trial should be conducted on 100 patients in the country. The PK study data should be submitted before the Committee for review.</p>
2.	Ceritinib Hard Gelatin Capsule 150	M/s. Novartis Healthcare	The treatment of patients with locally advanced or	Recommendation: After detailed deliberation, the Technical Committee recommended the waiver of local clinical trial

	mg	Pvt. Ltd	metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive	<p>as per the recommendation of the SEC.</p> <p>SEC Recommendation: The firm has applied for grant of permission to import and market the drug in the country with local clinical trial waiver. The firm has presented that the drug was approved in USA as an orphan drug for the said indication. Further the firm has submitted that ALK positive patients are only 3% of total NSCLC patients and hence would qualify as Orphan drug in the country. The firm has also presented the safety and efficacy data generated in other countries. The Committee deliberated the proposal in detail and recommended for import and marketing of the drug in the country subject to condition that the firm should actively follow up first 50 patients and collect safety and efficacy data and submit before the Committee</p>
NP	3. Ibutilide Fumarate Injection 0.1mg/ml	M/s Zuventus Healthcare Ltd	For the rapid conversion of atrial fibrillation or atrial flutter of recent onset to sinus rhythm	<p>Recommendation: After detailed deliberation, the Technical Committee recommended the waiver of local clinical trial as per the recommendation of the SEC.</p> <p>SEC Recommendation: In response to the SEC recommendation of 30/09/2014 the firm has requested for waiver of local clinical trial. Earlier the firm was granted NOC for conduct of clinical trial and it was further mentioned that after one year no patients could be recruited. The Committee deliberated on this issue and decided that the company should provide specific reason with evidence from all the approved centers, and comments for non-recruitment of the trial patients and as per SEC recommendation of 16.12.2014, the firm presented its proposal in detail, it was noted that the firm has not yet submitted the specific reason(s) for non-recruitment of subject in clinical trial from the five investigating sites with information to respective Ethics Committee by investigator(s) as communicated earlier. The SEC recommended that the firm may be asked to submit the above documents from all sites as per the recommendation of the SEC meeting held on 30.09.2014. In response the firm has submitted comments of 4 out of 5 investigators out of which 3 have categorically stated that they have not recruited any subject in the said study. One of the Investigator site has clearly sited difficulty in obtaining consent in emergent situations as the reason for non recruitment. The firm has submitted this in reply dated 15.01.2015. The Committee further deliberated on the matter in details. It was noted that 1. Atrial fibrillation / flutter is a condition needing urgent treatment 2. There is no satisfactory drug for pharmacological cardio version in this situation (Atrial fibrillation / flutter). 3. The said drug is approved by USFDA for the new onset atrial fibrillation since 1995. 4. In certain</p>

				specific situation like atrial fibrillation in post surgery patients and congenital heart disease, this is established as drug of choice. 5. Hence it may be categorized as a drug to be used in condition of extreme urgency category. Considering all the above conditions, the Committee recommended for a waiver of local clinical trial. The Committee however recommended that a Phase- IV clinical trial in minimum 120 patients be conducted. Accordingly the firm shall submit the protocol.
4.	Ibrutinib 140 mg Capsules	M/s Johnson & Johnson Ltd	For the treatment of Mantle cell Lymphoma, Chronic Lymphocytic Leukemia and Chronic Lymphocytic Leukemia with 17p deletion.	<p>Recommendation: After detailed deliberation, the Technical Committee recommended the waiver of local clinical trial as per the recommendation of the SEC subject to the condition that the firm shall submit outcome of the post-marketing trial annually till the completion of the study to DCG (I).</p> <p>SEC Recommendation: After detailed deliberation of the proposal the Committee observed the following:-</p> <ol style="list-style-type: none"> 1. The drug has been approved by USFDA, EMA, and Swiss medic as an orphan drug. The drug is indicated for the treatment of adult patients with Mantle Cell Lymphoma who have received at least one prior therapy, for the treatment of patients with chronic lymphocytic leukemia who have received at least one prior therapy and for the treatment of patients with chronic lymphocytic Leukemia with 17p deletion. 2. The firm presented data to show that the drug is effective in the above indications with acceptable toxicity. The drug will address the Unmet Medical Need of the Indian patients. However, the Committee noted that Indian patients have not yet been exposed to the drug. Therefore, the Committee recommended the waiver of the clinical trial and import and marketing permission of the drug with the condition that the firm shall conduct Phase IV clinical trial.
5.	Bovine lung surfactant-a drug powder lyophilisate for intratracheal instillation 54 mg/0.7 mL	M/s Bharat Serum and Vaccine Ltd	For the treatment of respiratory distress syndrome in the pre-term new born infants.	<p>Recommendation: After detailed deliberation, the Technical Committee recommended the waiver of local clinical trial as per the recommendation of the SEC.</p> <p>SEC Recommendation: The proposal was deliberated in the NDAC (Now renamed as SEC) in its meeting held on 28.01.2012</p> <p>Recommendation of SEC (Pulmonary): After detailed deliberation the Committee recommended that phase III clinical trial with the drug should be conducted. Accordingly protocol etc. should be submitted for consideration of the Committee. The protocol etc. would be deliberated in the next meeting. Two neonatologists should also be invited in the deliberation in the next meeting.</p> <p>The proposal of the firm was then referred to</p>

				<p>SEC vaccine where neonatologist was present</p> <p>Recommendation of SEC (Vaccine) 12.01.2015: The committee deliberated the proposal in detail. The firm has stated that the drug qualifies to be considered as Orphan Drug based on the published data and the firm has presented the proposed drug in a lyophilised formulation with better shelf life than the existing liquid formulation available in India and can be stored at 25°C. Further, the drug is reported to have been approved in Germany and many other countries.</p> <p>The committee recommended for the grant of Permission for Marketing Bovine Lung Surfactant in the Country with the condition that PMS data on at least 100 patients to be submitted within a year to get more safety data.</p>
6.	BST Car Gel	M/s Piramal Healthcare Pvt., Ltd	It is intended to promote hyaline cartilage regeneration when used in conjunction with the bone marrow stimulation technique such as microfracture or drilling for the repair of damaged articular cartilage in the adult knee	<p>Recommendation: After detailed deliberation, the Technical Committee recommended the waiver of local clinical trial as per the recommendation of the SEC.</p> <p>SEC Recommendation: The firm made a presentation before the committee. After detailed examination of the available clinical materials provided by the company, the committee came to the conclusion that permission for import & marketing of the product under Rule-122A of D & C Act & Rules may be granted with a condition to carry out Phase-IV clinical trial in Indian population. Accordingly the firm should submit the study protocol within a period of 6-months w.e.f. the date of approval for further deliberation in the SEC.</p>

Recommendation:

The Apex Committee deliberated the proposals and concurred with the recommendations of the Technical Committee for clinical trial waiver in respect of proposal no. 2, 4 and 6. The Apex Committee deferred proposals at sl. No. 1, 3 and 5 and Committee sought further details in respect of each of these proposals.

The meeting ended with vote of thanks to and from the chair.
