MINUTES OF THE 31st MEETING OF THE APEX COMMITTEE HELD ON 26-07-2016 UNDER THE CHAIRMANSHIP OF SECRETARY, (H&FW) 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. SOUMYA SWAMINATHAN**
   Secretary, DHR & DG ICMR
3. **Dr. JAGDISH PRASAD**
   DGHS
4. **SHRI K. L. SHARMA**
   Joint Secretary
   Department of Health and Family Welfare

Special Invitees:

1. **SHRI K. B. AGGARWAL**
   Addl. Secretary (F&D)
   Ministry of Health and Family Welfare
2. **Dr. G. N. SINGH**
   DCG (I), FDA Bhavan, New Delhi
3. **Dr. V. G. Somani**
   Joint Drugs Controller (I), CDSCO
4. **R. Chandrashekar**
   Dy. Drugs Controller (I), CDSCO

Initiating the discussion, Chairman, Apex Committee welcomed the members of the Committee and special invitees to the meeting. Thereafter, the Committee deliberated upon each of the agenda items and recommended as following:

Agenda items which had been postponed from the 30th Apex Committee meeting on 29.06.2016

ITEM No. 03

Proposals for Clinical Trial Waiver in Indian population for approval of new drugs falling under the category of drugs, which have already been approved outside India.

Proposal No.01:

Eltrombopag Olamine Tablets 25 mg/50 mg (Additional Indication).

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-I**).

Proposal No.02:

Bortezomib for injection 3.5 mg/vial and 1 mg/vial powder for injection (Additional Indication).

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-I**).

Proposal No.03:

Anagrelide 0.5 mg Capsules.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-I**).

OTHERS:

1. **Discussion on the proposal of M/s APAC Biotech Pvt. Ltd, Gurgaon for Marketing Authorization of APCEDEN™ [Dendritic Cell (DC) product].**

   The committee noted that various concerns have been raised on the safety and efficacy of the product and is also under the vigilance examination. Therefore the committee did not consider the proposal.

Additional Agenda for 30th meeting

1. **A Phase-II/III, Randomized, double-Masked, sham-controlled trial of QPI – 1007 delivered by single or multi-dose intra-vitreal Injection(s) to subjects with acute non-arteritic anterior ischemic optic neuropathy (NAION)**

   The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study (Details at **Annexure-II**).

2. **Medroxyprogesterone Acetate (MPA) 104 mg in 0.65mL suspension for injection**

   The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-III**).

Agenda items of 31st Apex Committee

ITEM No. 01

Proposals of Clinical Trials related to New Chemical Entities (NCEs) recommended by Technical Committee:

Proposal No.01:

Efficacy and long-term safety of Oral Semaglutide versus Sitagliptin in subjects with Type 2 Diabetes.

The committee noted that there is no definition for Phase IIIa clinical trial under Schedule-Y and therefore decided that the proposal should be treated as a Phase III clinical trial. The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study subject to the condition that the requirements for conduct of Phase-III clinical trial under Schedule-Y of Drugs and Cosmetics Act 1940 and Rules 1945 should be complied with (Details at **Annexure-IV**).

ITEM No. 02

Proposals for Clinical Trial Waiver in Indian population for approval of new drugs falling under the category of drugs, which have already been approved outside India.

Proposal No.01:

Pertuzumab Injection 420 mg/ 14 ml vial – (Additional Indication).

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-V**)

Proposal No.02:

Perampanel Tablets (2/4/6/8/10/ and 12mg).

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-V**) with the condition that post market surveillance be carried out as per terms and conditions of Schedule Y and the duration of PMS may be kept at two years.

Proposal No.03:

Minocycline Extended Release Tablet 45/65 mg (Additional Dosage).

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-V**). The Committee further directed that an analysis be carried out to ascertain the reasons why the approval of the proposal has taken such a long time.

Proposal No.04:

Dolutegravir 50 mg Tablets.

The Apex Committee, after detailed deliberations, based on the recommendations of the Technical Committee and NACO, recommended for grant of permission for manufacturing and marketing in the country with local clinical trial waiver with the

condition that a Phase-IV clinical trial be conducted after approval of drug in the country (Details at **Annexure-V**).

Proposal No.05:

Carfilzomib Injection, 60 mg/vial.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-V**).

Proposal No.06:

Lenvatinib 4 mg/10 mg Capsules.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-V**).

OTHERS:

The Committee deliberated upon the procedure adopted for the grant of permission/approval of drugs for marketing in the country as provided under the Drugs and Cosmetics Rules, 1945. The Committee noted that provisions are available under the Rules to abbreviate, omit, modify or relax submission of non-clinical and clinical data in case of new drugs approved and marketed in other countries for several years. Therefore the Committee opined that Conduct of local clinical trials should not be necessary condition in case of drugs already approved in USA, UK, EU, Japan, Australia and Canada. However, these should be subjected to the a robust post marketing surveillance for not less than two years in the country.

The Committee also noted that in cases relating to change in the route of administration local clinical trial may not be insisted upon provided similar route of administration has already been approved in USA, UK, EU, Japan, Australia and Canada.

It was decided that these proposals may be draft notified for inviting comments of stakeholders and, the policy may, thereafter be finalized after considering comments.

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

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Annexure-I

Recommendations of the 03 cases of Clinical trial waiver in Indian populations of 33rd Technical Committee Meeting held on 20.05.2016.

S.No.	Details of the Drug	Indication	1. Recommendations of the Technical Committee 2. Recommendations of the SEC.
1.	Eltrombopag Olamine Tablets 25 mg/50 mg **(Additional Indication)** **Date of Application:** M/s Novartis Healthcare Pvt. Ltd (Application date: 23.03.2016, initial application was made by M/s GSK dated: 01.05.2015). **Name of the Firm:** M/s Novartis Healthcare Pvt. Ltd **Regulatory status in India:** Approved on 19.10.2010 for treatment of thrombocytopenia in patients with chronic immune (idiopathy) thrombocytopenic purpura who have had insufficient response to corticosteroids immunoglobulin or splenectomy. (It should be used only in patients ITP whose degree of	Treatment of cytopenias in patients with severe aplastic anemia (SAA) who have had an insufficient response to immunosuppressive therapy	**Recommendation of the SEC Oncology & Haematology) held on 07.04.2016:** The firm presented the clinical trial data on use of Eltrombopag Olamine in the treatment of cytopenias in patients with Severe Aplastic Anaemia (SAA) who have had an insufficient response to immunosuppressive therapy. The drug is already approved for the same in USA and EU, and also has Orphan drug status. After detailed deliberation the committee recommended for the proposed additional indication (the treatment of cytopenias in patients with severe aplastic anemia (SAA) who have had an insufficient response to immunosuppressive therapy). **SEC Expert List:** **1.** Dr. Sameer Bakshi, Professor, Dept. of Medical Oncology, AIIMS, New Delhi. **2.** Dr. Hemant Malhotra, Head, Division of Medical Oncology, SMS Medical College, Jaipur **3.** Dr. C. K. Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata **4.** Dr. (Brig.) Ajay Sharma, Professor, Dept of Hematology, Army Hospital (Research &

	thrombocytopenia and clinical condition increase the risk for bleeding, should not be used in an attempt to normalise platelet counts) **Regulatory status in other countries:** EU, USA & Australia		Referral), Dhaula Kuan, New Delhi, Delhi 110010 **5.** Dr. H.P Pati, Department of Oncology, AIIMS, New Delhi. **6.** Dr. D S Arya, Prof., Dept. of Pharmacology, AIIMS, New Delhi. **7.** Dr. Raju Titus Chacko, Professor & Head, Department of Medical Oncology, Christian Medical, College, Vellore- 632004 **8.** Dr. V Anand, HOD, Department of Vascular surgery, Army Hospital, New Delhi. **9.** Dr. Anurag Srivastava, Prof & Head, Department of surgical Disciplines, AIIMS, New Delhi. **Recommendations of the Technical Committee held on 20.05.2016:** After detailed deliberations, the Committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
2.	Bortezomib for injection 3.5mg/vial and 1mg/vial powder for injection **(Additional Indication)** **Name of the Firm:** M/s Johnson & Johnson Pvt. Ltd **Date of Application:** 18.12.2015	For the treatment of patients with mantle cell lymphoma	**1. Recommendation of the SEC (Oncology) held on 15.03.2016:** The committee noted that the drug is being marketed in India since 2005 and for indication "for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy" drug is used since 2007. Based on the data from pivotal study conducted globally since 2008, the committee recommended approval of additional indication i.e. treatment of patients with

	Regulatory status in India: Approved on 19.05.2005 for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy **Regulatory status in other countries:** EU, USA &Australia		mantle cell lymphoma. **SEC Expert List:** **1.** Dr. Sameer Bakshi, Professor, Dept. of Medical Oncology, AIIMS, New Delhi **2.** Dr. Sanjay Kumar Singh, , Dept. of Medical Oncology, Gajara Raja Medical College, Veer Savarkar Marg, Gwalior **3.** Dr. S.D. Banavali, Head, Dept. of Medical Oncology, Tata Memorial Hospital, Parel, Mumbai-400 012 **4.** Dr. Geeta Narayanan, Professor, Dept. of Medical Oncology, Regional Cancer Centre, Trivandrum- 695011 **5.** Dr.Urmila Thatte, Prof. and Head, Dept. of Clinical Pharmacology, SGS Medical College, KEM Hospital, Mumbai.-400012 **2. Recommendations of the Technical Committee held on 20.05.2016:** After detailed deliberations, the Committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
3.	Anagrelide 0.5 mg Capsules **Date of Application:** 15-10-2015 **Name of the firm:** M/s. Cipla Ltd. **Regulatory status in**	Indicated for the treatment of patients with thrombocythemia, secondary to myeloproliferative neoplasms, to reduce the elevated platelet count and the risk	**1. Recommendation of the SEC (Oncology & Hematology) held on 07.04.2016** The Committee deliberated the proposal in detail and recommended for local clinical trial waiver with the conditions i) that the drug should be used as a second line therapy "for the reduction of elevated platelet counts in at risk essential thrombocythemia patients who are intolerant to their current therapy or whose platelet counts are not

	India: Not approved in India **Regulatory status in other countries:** USA & UK	of thrombosis and to ameliorate associated symptoms, including thrombo-haemorrhagic events	reduced to an acceptable level by their current therapy" as approved in EU. ii) The BE study should be conducted in statistically significant number of subjects as per the protocol presented before the Committee. **SEC Expert List:** **1.** Dr. Sameer Bakshi, Assistant Professor, AIIMS, New Delhi **2.** Dr. Hemant Malhotra, Head, Division of Medical Oncology, SMS Medical College, Jaipur **3.** Dr. C. K. Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata **4.** Dr. (Brig.) Ajay Sharma, Professor & Senior Advisor, Army Hospital (Research & Referral), New Delhi **5.** Dr. Raju Titus Chacko, Professor & Head, Department of Medical Oncology, Christian Medical, College, Vellore **6.** Dr. H.P. Pati, AIIMS, Ansari Nagar Delhi **7.** Dr. D S Arya Professor, Department of Pharmacology AIIMS, New Delhi. **8.** Dr. V Anand, HOD, Dept of Vascular Surgery, Army Hospital, New Delhi. **9.** Dr. Anurag Srivastava, Prof & Head, Department of Surgical Discipline, AIIMS, New Delhi. **2. Recommendations of the Technical Committee held on 20.05.2016:** After detailed deliberations, the Committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.

Annexure-II

Proposal of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee.

S.No.	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	1. Recommendation of the Subject Expert Committee /IND Committee 2. Recommendation of the Technical Committee
1.	**Name of the Drug:** QPI-1007 **Protocol No**: QRK207 **Name of the Applicant**: Manipal AcuNova Limited Mobius Towers, SJR i-Park Whitefield, EPIP Bangalore – 560066. Karnataka, India. **Name of the Sponsor**: Quark Pharmaceuticals, Inc, 6501 Dumbarton Circle, Fremont, CA 94555, USA **Name of the Manufacturer**: **Active pharmaceutical ingredient (API):** Agilent Technologies, Inc. 5555 Airport Road Boulder, CO	**Risk Vs Benefits to the patients:** The Risk Vs Benefits profile of the test drug from pre clinical single, repeated dose toxicity studies, genotoxicity and phase I clinical study justify the conduct of study. **Innovation vis a vis existing therapeutic option:** The purpose of the study is to assess the safety, efficacy and tolerability of QPI-1007 administration as three bimonthly intravitreal injections on visual acuity in subjects with recent onset NAION. **Unmet Medical Need in the Country**: NAION is an unmet medical need. There are no therapeutic options currently approved for the disease.	**Recommendation of the SEC:** The initially approved protocol was version 02. The firm now requested for certain amendments vide **protocol version 05 dated 16.10.2015**. After detailed deliberations the committee recommended approval of version 05. Further the firm made an oral request for increasing the number of patient from India from 120 to 160. However the committee felt that the increase in number of subjects, at this stage, is not called for. **(Dr. Rohit Saxena did not participate in the deliberations.)** **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of

	80301 USA **Finished Formulation:** Albany Molecular Research Inc (AMRI) Burlington: 20 Blanchard Rd Burlington, MA 01803 USA. **Title:** A Phase 2/3, Randomized, Double-Masked, Sham-Controlled Trial of QPI-1007 Delivered By Single or Multi-Dose Intravitreal Injection(s) to Subjects with Acute Nonarteritic Anterior Ischemic Optic Neuropathy (NAION).		the study.

Annexure-III

Medroxyprogesterone Acetate (MPA) 104 mg in 0.65mL suspension for injection

S.No	Details of the Proposal	Indication	1. Recommendation of the Subject Expert Committee (SEC)/IND Committee 2. Recommendation of the Technical Committee
1.	Medroxyprogesterone Acetate (MPA) 104 mg in 0.65mL suspension for injection **Name of the Applicant:** M/s. Pfizer Products India Pvt. Ltd. **Regulatory status:** The drug is approved for the applied indication through another route of administration (IM) and strength in the country. The proposed formulation is approved in US, Pakistan, Bangladesh etc..	For long term female contraception.	**Recommendation of NDAC (Reproductive and Urology) on 23.01.2014:** The committee opined that this particular formulation is being marketed in various countries and it is also recommended by WHO. The proposed formulation is a reduced dose than I.M dose. This delivery system is novel and it is convenient for use when compared to I.M. Drug (Medroxyprogesterone Acetate (MPA) 150mg/mL suspension for injection) and the safety and efficacy of the drug is already established. Therefore committee recommended for import and marketing of MPA 104mg in 0.65mL subject to submission of PSUR every six month to the office of DCG(I). **Recommendation of the Technical Committee:** The proposal was deliberated in Technical Committee on 13-10-2014 where the Committee after detailed deliberation agreed to the recommendations of the SEC for marketing authorization of the drug without conducting local clinical trial. **Recommendation of the Apex Committee:** The proposal was deliberated in Apex Committee on 15-10-2014 where the Committee recommended that the Technical Committee should specifically mention if this case falls under the five criteria laid down for waiver of local clinical trial in Indian populations for approval of new drugs 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. **Re-deliberation in SEC:** The proposal for addition of indication (for long term female contraception) was deliberated in 11th SEC (Reproductive and urology) meeting held on 27-02-2015 for additional indication i.e long-term female contraception. The SEC noted that MPA, 104 mg in 0.65mL, SC is already approved for management of endometriosis. Firm has requested for additional indication for long term female contraception and informed that this product is already approved internationally (USA, UK etc.,) for the proposed indication. The committee recommended for approval of the indication i.e. for long term female contraception without conducting clinical trial as it is satisfactory subcutaneous therapy for the proposed indication which is not yet available in the country and further dose is also reduced with SC route when compared to IM route. **Re-deliberation in Technical Committee:** The proposal for import and marketing of Medroxyprogesterone Acetate (MPA) 104mg in 0.65mL Suspension for Injection for long term female contraception was deliberated in 24th Technical Committee on 06.05.2015 where committee noted that there are various alternatives available in respect of the proposed additional indication and being a sub-cutaneous route which is new for its use and operationalization for the purpose of contraception, the Committee recommended that a phase III trial shall be conducted.

			Re-deliberation in Technical Committee based on the request by the firm: The firm has made a presentation before the Committee and the following three subject experts: 1. Dr. Sudha Prasad, HOD, Dept. of Gynaecolo MAMC, New Delhi. 2. Dr. Alka Kriplani, HOD, Dept of Gynaecolo AIIMS, New Delhi. 3. Dr. Indu Chawla, Dept. of Gynaecology Obstetrics in Dr. Ram Manohar Lohia Hospital (RML) Delhi. The subject experts opined that subcutaneous route is a better option over the Intramuscular route as lower dose of the drug is required and also because of convenience for use. Further, the drug is approved for the applied indication through subcutaneous route in 38 countries. The Committee also noted that pivotal study for the same indication through subcutaneous route has been conducted in Asian countries like Bangladesh and Pakistan which has demonstrated the safety and efficacy of the drug. Therefore, the Committee agreed with the opinion of the subject experts and recommended for waiver of local clinical trial.

Annexure-IV

Proposal of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee in its 34th Meeting held on 15.07.2016.

Proposal No	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	1. Recommendation of the Subject Expert Committee (SEC)/IND Committee 2. Recommendation of the Technical Committee
1.	**Name of the Drug:** Oral Semaglutide **Date of Application:** 07/Dec/2015 **Protocol No**: NN9924-4222 **Phase of the trial:** IIIa **Name of the Applicant:** Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore - 560 066, Karnataka, India. **Name of the Sponsor:** Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore - 560 066, Karnataka, India. **Name of the Manufacturer:** Novo Nordisk A/S, Novo Allé, DK-2880, Bagsværd, Denmark.	**Risk versus benefit to the patients-** The safety profile of the test drug from preclinical toxicity studies including repeat dose toxicity, genotoxicity, carcinogenicity studies and clinical phase I, II studies justify the conduct of the study. **Innovation vis-a-vis existing therapeutic option** The purpose of study is to compare efficacy and long-term safety of oral Semaglutide versus Sitagliptin in subjects with type 2 diabetes. **Unmet need in the country-** The test drug may be an alternative treatment option in subjects with type-2 diabetes.	**The proposal was deliberated in SEC (Endocrinology) held on 22-03-2016:** After detailed deliberation the committee noted that there is no justification for dose escalation irrespective of glycemic control. It should be based on glycemic target rather than fixed dose escalation. Subjects with fasting glucose level more than 270mg/dl at the time of randomization should be excluded from the study. Hence the committee did not recommend the conduct of the study in its presented form. **The proposal was re-deliberated in SEC (Endocrinology) held on 14-06-2016:** The proposal was deliberated in SEC held on 22/03/2016. After detailed deliberation the committee noted that there is no justification for dose escalation irrespective of glycemic control. It should be based on glycemic target rather than fixed dose escalation. Subjects with fasting glucose level more than 270mg/dl at the time of randomization should be excluded from the study. Hence the committee did not

	Title: Efficacy and Long-Term Safety of Oral Semaglutide Versus Sitagliptin in Subjects with Type 2 Diabetes.		recommend the conduct of the study in its presented form. After detailed deliberation, the justification furnished by the firm was found acceptable. The committee recommended the conduct of the study subject to the condition that the OADs be provided free of cost. Accordingly, the firm has submitted the undertaking. **SEC Expert:-** **1)** Dr. Rajesh Khadgawat, Associate Prof., Dept. of Endocrinology, AIIMS, New Delhi-110029. **2)** Dr. Rajesh Rajput, Senior Prof. & Head Dept. Endocrinology & Medicine VI PFIMS, Medical Road, Rohtak-124001. **3)** Dr. D. S. Arya, Prof. Dept. of Pharmacology, AIIMS, New Delhi. **4)** Dr. Manoj Chadha, dept. of Endocrinology P.D Hinduja National Hospital Mahim, Maharashtra-400016. **5)** Dr. Richa Dewan, Dept. of Medicine, Maulana Azad Medical College, New Delhi. **Recommendation of the Technical Committee on 15.07.2016:** After detailed deliberation, the Committee agreed with the SEC and recommended for the approval of the study.

Annexure V

Recommendations of the 06 cases of Clinical trial waiver in Indian populations of 34th Technical Committee Meeting held on 15.07.2016.

S.No.	Details of the Drug	Indication	1. Recommendations of the SEC. 2. Recommendations of the Technical Committee
1.	**Name of the Drug:** Pertuzumab Injection 420 mg/ 14 ml vial – (**Additional Indication)** **Date of Application:** 14.01.2016 **Name of the Firm:** M/s Roche India Pvt. Ltd., Mumbai **Regulatory status in India:** Approved dated 29.12.2014 for the indication "Pertuzumab is indicated combination with Trastuzumab and Docetaxel for patients with HER-2 positive metastatic or locally recurrent unresectable breast cancer, who have not received any chemotherapy for their metastatic disease **Regulatory status in other countries for the**	In combination with Trastuzumab and chemotherapy for the neoadjuvant treatment of patients with HER2 positive, locally advanced, inflammatory, or early stage breast cancer (either >2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer"	**Recommendation of SEC (Oncology) held on 24.05.2016:** The committee noted that the drug Pertuzumab is approved in the neoadjuvant setting in combination with Trastuzumab and chemotherapy in locally advanced breast cancer by USFDA and 60 other countries. The drug has demonstrated significant benefit in this setting with potential to save lives. The firm also presented safety data on 37 Indian patients from ongoing Phase IV clinical trial, and no additional safety signals have been noted. Based on this data provided by firm the SEC recommended the approval of additional indication with local clinical trial waiver in the proposed indication. **SEC Experts:-** **1)** Dr. Sameer Bakshi, Professor, Dept. of Medical Oncology, AIIMS, New Delhi. **2)** Dr. Sanjay Kumar Singh, Dept. of Medical Oncology, Gajara Raja Medical College, Veer Savarkar Marg, Gwalior. **3)** Dr. S. D. Banavali, Head, Dept. of Medical Oncology, Tata Memorial Hospital, Parel, Mumbai **4)** Dr. Geeta Narayanan, Professor, Dept. of Medical Oncology, Regional Cancer Centre, Trivandrum.

	proposed Indication: USA, UK, EU and Japan		**Recommendation of the Technical Committee on 15.07.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
2.	**Name of the Drug:** Perampanel Tablets (2/4/6/8/10/ and 12 mg) **Date of Application**: 01.04.2013 **Name of the Firm:** Eisai Pharmaceuticals India Pvt. Ltd. **Regulatory status in India:** Not Approved **Regulatory status in other countries:** EU and USA	Perampanel is a non-competitive AMPA glutamate receptor antagonist, is indicated as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy aged 12 years and older	**Recommendation of SEC (Neurology and Psychiatry) held on 18.03.2016:** The committee made the following recommendations: Earlier the proposal of the firm was deliberated in the SEC twice and the Committee recommended the firm to conduct phase-III clinical trial as the data presented was not sufficient. During the present deliberation following clarification were sought by the Committee: **i.** The retention rate of the patients in the trials and reasons for high dropout rates. **ii.** The efficacy shown with 8mg and12mg should be supported with PK/PD data. **iii.** All the reported SAEs including death should be submitted with causality assessment to DCG (I) office. **iv.** The number of Indian patients in the global trial within the dose groups (2/4/6/8/12 mg/day) are too few for any valid statistical conclusion. Therefore, the Committee recommended that the firm is required to conduct a phase-III trial in adequate number of patients. **SEC Experts:-** **1)** Dr. Bhavna Kaul, Head, Dept. of Neurology, VMMC, New Delhi. **2)** Dr. M. S. Bhatia, Prof and Head Dept. of Psychiatry, UCMS, New Delhi.

			3) Dr. R. Smita N Deshpande, Prof and Head, Dept. of Psychiatry, RML Hospital, New Delhi. **4)** Dr. Sunil K. Narayan, Prof and Head, Department of Neurology, JIPMER, Puducherry. **5)** Dr. Debashish Chowdhury, Professor of Neurology, MAMC, New Delhi **6)** Dr. K. H. Reeta, Dept. of Pharmacology, AIIMS, New Delhi. **7)** Dr. M. V. Padma, Department of Neurology, AIIMS, New Delhi. **8)** Dr Bikash Medhi, Dept. of Pharmacology, PGIMER, Chandigarh The proposal was deliberated in the Technical Committee in view of its representation. **Recommendation of Technical Committee on 15.07.2016:-** The firm has conducted a Global Clinical Trial in which India was one of the site. A total of 115 Indian Patients participated in Phase II and III clinical trials. The drug is first is in its class with different mechanism of action when compared to the available drugs. The drug is indicated for Refractory partial onset seizures which is an Orphan condition and if left untreated may lead to progressive brain damage in patients leading to increased morbidity and mortality. The drug is approved in 47 countries including EU, US, Japan, Australia, Singapore, Malaysia, and Taiwan. Therefore the Committee recommended for import marketing of the drug with local clinical trial waiver subject to condition that the firm shall conduct a Post Marketing Surveillance study for a period of one year

			from the date of launch of the product in the market.
3.	**Name of the Drug:** Minocycline Extended Release Tablet 45/65 mg **(Additional Dosage)** **Date of Application:** 19.12.2012 **Name of the Firm:** M/s Sun Pharmaceuticals Private Limited. **Regulatory status in India:** Approved (100mg) **Regulatory status in other countries:** USA	Minocycline is prescribed for the treatment of acne viz. inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age or older	**Recommendation of SEC (Dermatology & Allergy) held on 22.06.2016**, where firm presented the data before the committee and after detailed deliberation the committee noted that- **a)** Minocycline ER Tablet 45/65 mg is approved in U.S.A for the proposed indication. **b)** The higher strength (100mg) of the same product is already approved in India for the treatment of acne. **c)** The excipients used in the proposed ER formulation are same as approved in U.S.A. **d)** The efficacy is similar to 100 mg IR formulation while the AE reported with the Minocycline ER Tablet 45/65 mg is comparatively better. In view of the above the committee is of the opinion that clinical trial will not generate any new data and recommended the manufacturing and marketing of Minocycline ER Tablet 45/65 mg for the indication of treatment of acne viz. inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age or older with the condition that package insert should highlight all the AE's in bold letters. **SEC Experts:-** **1)** Dr. V. K. Sharma, Professor and Head, Dept. of Dermatology, AIIMS, New Delhi. **2)** Dr. D. M. Thappa, Professor and Head,

			Dept. of Dermatology, JIPMER, Pondicherry. **3)** Dr. S.N. Bhattacharya, Prof & Head, Dept. of Dermatology, University College of Medical Sciences, New Delhi. **4)** Dr. Shalini Chawala, Prof. Dept. of Pharmacology, MAMC, New Delhi. **Recommendation of the Technical Committee on 15.07.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
4.	**Name of the Drug**: Dolutegravir 50 mg Tablets **Date of Application:**14.03.14, 04.02.15, 22.03.16, 27.05.16 **Name of the Firm: M/s. Aurobindo Pharma,** [M/s Hetero Labs, M/s Emcure and M/s Mylan] **Regulatory status in India:** Not Approved **Regulatory status in other countries:** EU, USA and Canada	Antiretroviral - Dolutegravir (DTG) is a next-generation HIV integrase strand transfer inhibitor (INSTI). Dolutegravir is indicated in combination with other antiretroviral agents for the treatment of HIV infected adults and adolescents above 12 years of age.	**Recommendation of SEC (Antimicrobial and Antiviral) held on 23.05.2016:** The firm presented Global safety and efficacy data without any Indian patients, with the request for the waiver of clinical trial. After detailed deliberation the committee opined that **1.** There is no Indian subject data in the global clinical trials. **2.** Marketing authorization permission granted in US and Europe in 2013-14 and sufficient post marketing safety data are not available for the drug. **3.** At present there are alternate drugs available for the proposed indication **4.** Additionally, the drug doesn't meet the criteria specified for clinical trial waiver Therefore, the Committee recommended that the firms should conduct clinical trial in Indian subjects. **SEC Experts:-** **1)** Dr. Archana Thakur, Director and

			Professor, Dept. of Microbiology, G B Pant Hospital, Jawaharlal Nehru Marg, New Delhi. **2)** Dr. C.D Tripathi, Professor, Head, Department of Pharmacology, VMMC, New Delhi **3)** Dr. B. Gupta, Dept. of Medicine, NDMC & Hindu Rao Hospital, New Delhi. **4)** Dr. Amita Jain, Professor, Dept. of Microbiology, KGMC, Lucknow. **5)** Dr. Abhishek Agarwal, Dept. of Medicine, SMS Medical College, Jaipur. **6)** Dr. Manish Bamrotiya, NACO. **Re-deliberation in the SEC (Antimicrobial and Antiviral) held on 14.07.2016:** The proposal is placed before the SEC committee for deliberation and the Committee sought the data on advantages with respect to efficacy, mutation and rapid reduction in viral load which firm have said that it is available and will be provided. The major observation of the Committee include: **1.** Documentary evidence with data on better safety profile and lesser adverse events (AEs) with respect to CNS activity, psychiatric disorder, rashes, diarrhoea of Dolutegravir along with comparative statement on AEs & lower rate of discontinuation than Efavirenz following sustained treatment. Also reported suicidal cases on Efavirenz which may lead to replacement of the drug with Dolutegravir as preferred treatment rather than alternate treatment as per WHO guideline 2016 on HIV treatment. These

			statements must be supported with data and references. **2.** Report with supportive data on the comparative drug-drug interaction of all the anti-HIV drugs & the safety profile of Dolutegravir with information on drug-drug interaction especially those with clinical importance and common. **3.** Justification on the claim that Dolutegravir is indicated in adults and children aged 12 years and older and weighing at least 40 kg, and how it would be relevant in the Indian patient scenario. **4.** If the proposal is considered initially for adults, what would be the response of firms? As the representative from NACO was not present, the Committee also opined to obtain the opinion of the NACO on the essentiality and desirability of the drug. The Committee recommended the proposal for waiver of local clinical trial with condition that Phase IV clinical trial in 250 patients shall be conducted after approval of the drug in the country. **SEC Experts:-** **1)** Dr Y K Gupta, Professor, Department of Pharmacology, AIIMS, New Delhi **2)** Dr. Archana Thakur, Director and Professor, Dept. of Microbiology, G B Pant Hospital, Jawaharlal Nehru Marg, New Delhi. **3)** Dr. B. Gupta, Dept. of Medicine, NDMC & Hindu Rao Hospital, New Delhi. **4)** Dr Varsha Gupta, Professor, Department of Microbiology. GMCH, Chandigarh

			5) Dr. S K Sharma, Professor, Department of Medicine, AIIMS, New Delhi. **Recommendation of the Technical Committee on 15.07.2016:-** The Committee recommended that the clarifications sought by SEC about data and opinion from NACO shall be obtained separately and the CDSCO shall evaluate the same. The approval shall be given if there are no specific observations, which indicates compulsory conduct of Phase III clinical trial, as the drug is already approved in more than 99 countries including US, UK. Finally, the Committee recommended the proposal as per recommendation of SEC for waiver of local clinical trial with condition that Phase IV clinical trial in 250 patients shall be conducted after approval of the drug in the country. **Opinion of NACO dated 22.07.2016:** NACO agreed with the recommendations of the Technical Committee for waiver of local clinical trial with the condition that phase-IV clinical trial in 250 patients shall be conducted after approval of the drug.
5.	**Name of the Drug**: Carfilzomib Injection, 60mg/vial **Date of Application:** 31.03.16 **Name of the Firm:** M/s. Amgen Technology Pvt. Ltd	Relapsed or Refractory Multiple Myeloma Carfilzomib (Krprolis®) for Injection is indicated in combination with	**Recommendation of SEC (Oncology) held on 28.06.2016:** The firm has applied for import and marketing of Carfilzomib for injection 60 mg/vial in the country for the proposed indication. The firm has made its presentation before the committee for marketing of the drug with local clinical trial waiver. The firm submitted that the drug was designated as orphan drug by USFDA and

	Regulatory status in India: Not Approved **Regulatory status in other countries:** USA, European Union, Argentina, Columbia, Israel, Mexico, Kuwait, Canada, Switzerland, South Korea and Thailand	dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who received one to three lines of therapy. Carfilzomib (Krprolis®) for Injcetion is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who received one to three lines of therapy.	EMA. The Committee deliberated in details the proposal and noted that there are no satisfactory therapies for multiple myeloma and opined that the drug is suitable candidate for orphan status in the country. Therefore the Committee recommended for import and marketing of the drug with local clinical trial waiver subject to the following condition: **1)** A structured Phase IV clinical trial with defined inclusion and exclusion criteria should be conducted. **2)** The disease response evaluation should be done as per standard procedure. **3)** The no. of patients enrolled should not be less than 100. **4)** All provisions of Schedule Y should be complied with. The protocol should be submitted to the office of DCGI within six months from the date of approval for marketing the drug in the country. **SEC Experts:-** **1)** Dr. Sameer Bakshi, Professor, Dept of Medical Oncology, AIIMS, New Delhi. **2)** Dr. Hemant Malhotra, Head, Division of Medical Oncology, SMS Medical College, Jaipur. **3)** Dr. C. K Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Institute, Kolkata. **4)** Dr. Sanjay Kumar Singh, Dept. of Medical oncology, Gajara Raj Medical College, Veer Savarkar Marg, Gwalior. **5)** Dr. D. S. Arya, Dept of Pharmacology, AIIMS New Delhi. **Recommendation of the Technical Committee on 15.07.2016:** After detailed

			deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
6.	**Name of the Drug**: Lenvatinib 4 mg/10 mg Capsules **Date of Application**: 24.09.2015 **Name of the Firm:** M/s. Eisai Pharmaceuticals India Private Ltd. **Regulatory status in India:** Not Approved **Regulatory status in other countries:** US, Europe and Japan	For the treatment unresectable thyroid cancer	**Recommendation of SEC (Oncology) held on 28.06.2016:** The firm has applied for import and marketing of the drug Lenvatinib 4mg/10mg Capsules which is indicated for the treatment of unresectable thyroid cancer. The firm has made its presentation before the Committee for marketing of the drug with local clinical trial waiver. The firm submitted that the drug was designated as orphan drug by USFDA, Japan and EMA. The Committee deliberated in detail the proposal and noted that there are no satisfactory therapies for patients of differentiated thyroid cancer who have metastasis and have progressed after radioactive iodine therapy and opined that the drug is suitable candidate for orphan status in the country with local clinical trial waiver. Notably, there is no phase III data to support the use of the drug in medullary or anaplastic thyroid cancer. Therefore the Committee recommended for import and marketing with local clinical trial waiver for the indication "locally recurrent metastatic progressive radioactive iodine refractory differentiated thyroid cancer". subject to the following conditions: 1 A structured Phase IV clinical trial with defined inclusion and exclusion criteria should be conducted. 2 The disease response evaluation should be done as per standard procedure. 3 All provisions of Schedule Y should be complied with.

			The protocol should be submitted to the office of DCGI within six months from the date of approval for marketing the drug in the country. **SEC Experts:-** **1)** Dr. Sameer Bakshi, Professor, Dept of Medical Oncology, AIIMS, New Delhi. **2)** Dr. Hemant Malhotra, Head, Division of Medical Oncology, SMS Medical College, Jaipur. **3)** Dr. C. K. Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Institute, Kolkata. **4)** Dr. Sanjay Kumar Singh, Dept. of Medical oncology, Gajara Raj Medical College, Veer Savarkar Marg, Gwalior. **5)** Dr. D. S. Arya, Dept of Pharmacology, AIIMS New Delhi. **Recommendation of the Technical Committee on 15.07.2016:-** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.

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