1. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 14.01.2012:-

The NDAC (Cardiology and Renal) deliberated the proposals on 14.01.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG	RECOMMENDATIONS
1	**Nutrineal PD4 + Amino Acid**	The committee discussed in detail and pointed out that the clinical data although shows improvement in biochemical parameters like albumin, approval in major countries like Australia, UK, EU etc, no data was presented to show clinical benefit like reduction in infection and hospitalization. The experts felt that drug is important in CAPD patients as poor nutrition is the major problem and reason for high morbidity and has a advantage of no additional requirement of nutrition through external route, hence additional toxicity data may not required. One of the Clinical trial on 311 patients (Jonstone J. S, Leonar. J E et al study) referred by the firm might have assessed the above mentioned clinical end point, however detailed data was not presented before the committee. In view of above the committee recommended the approval of the product subject to following: 1. Submit Johnstone. J. S, Leonar. J E et al study data and assessment on clinically significant end point as reduction in infection rate and hospitalization. 2. Submit phase IV trial protocol within one month of approval having statistically significant subject number with assessment of reduction in infection rate and or hospitalization. Phase IV study should be initiated within 6 months of approval.
2	**Aliskiren + Amlodipine + Hydrochlorothiazide**	1. The International Regulatory Agency is reviewing Aliskiren containing medicines to assess the impact of data coming from the ALTITUDE study which was terminated. The study was conducted in type 2 Diabetes patients at high risk of fatal and non fatal cardiovascular and renal events. On the basis of primary interim analyses, the Data Monitoring committee concluded that study patients were unlikely to benefit from aliskiren. Furthermore there was a higher incidence of adverse events related to non fatal stroke, renal complications, hyperkalemia and hypotension in this high risk population. Additional analyses from ALTITUDE are ongoing and updated advice may be issued early in 2012 as confirmed by the firm. In view of above the committee did not recommend for approval at this stage. After completion of review by the International Regulatory Agency and data from ALTITUDE study data made available, NDAC may discuss the matter in

		due course of time.
3	**Tolvaptan**	Recommended for approval for manufacture and marketing the drug in the country without local clinical trial as it is a drug for unmet need in Indian patient. However before formal approval the firm should generate satisfactory single dose bioequivalence data. Further, Post marketing Phase IV trial should be carried out after getting protocol etc. approved from DCG (I).
4	**Ticagrelor**	Regarding need for Pharmacokinetic data in Indian population, during presentation, it was told by the sponsor that the drug has wide safety margin. They were asked to provide the data of safety margin. Committee based on data on global/Indian patients, recommended the marketing approval of drug for early availability.
5	**TRV120027**	The firm was not able to attend the meeting for making technical presentation. The data submitted by the firm was discussed. There was only seven days repeated dose toxicity data in rats and dogs which is not adequate as per Schedule Y. There is only one Phase-I study data. As safety data is inadequate, the committee did not recommend the study in India.
6	**VAL489**	1. As per the protocol during washout of 35 days for all RAAS blockers [Angiotension Receptor Blockers (ARB), Angiotensin Converting Enzyme inhibitors (ACE inhibitors), Direct Renin Inhibitors (DRI)] must be discontinued in children which is not acceptable. 2. One of the secondary objective is to assess the effect of Valsartan and Valsartan-bases treatments on proteinuria and eGFR in a subset of children with hypertension and chronic kidney disease. However parameters with respect to proteinuria are not going to be assessed at the time of enrollment. The company representative have expressed their inability to amend the protocol as above. In view of above the committee did not recommend for approval of the study in its present form.
7	**Eprotirome**	Recommended for approval subject to the following conditions:- i) Subjects aged ≥18 yrs and ≤65 yrs should be enrolled in the study. Carcinogenicity study data should be submitted as and when completed.

2. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 21.04.2012:-

The NDAC (Cardiovascular and Renal) deliberated the proposals on 21.04.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG	RECOMMENDATIONS
1	**Moexipril HCL 7.5mg and 15mg tablet**	Committee recommended for the clinical trial & BE study subject to condition that the trial should be comparative study of Moexipril vs. Perindopril. 50% of the trial sites should be multispecialty hospitals and the sites should be geographically distributed in the country. Revised protocol should be submitted to DCG(I) for his approval. Clinical trial and BE study reports when completed should be placed before the committee for consideration of proposal for approval of the drug.
2	**Azelnidipine Tab. 8mg / 16mg**	Most of the published reports of clinical trial presented are comparative studies of 8-16 mg of Azelnidipine OD versus Amlodipine 2.5-5mg od whereas amlodipine is used upto 10mg OD. Available clinical data on Azelnidipine is limited. The drug is marketed only in Japan. Committee recommended that a comparative noninferiority clinical trial of Azelnidipine versus amlodipine 10 mg od in statistically significant number of subjects should be conducted. Accordingly, revised protocol, detail of sites etc. should be placed before the committee for further consideration.
3	**Colesevelam HCl powder for oral suspension 1.875gm & tablet 625mg**	Committee recommended for giving permission to market the drug subject to condition that product label, package insert and promotional literature should contain the following box warning: “Patients with hypertriglyceridemia should be monitored carefully”.
4	**Hydrochlorothiazide CR Tablets 12.5 mg**	Committee recommended for the clinical trial & BE study. Clinical trial and BE study reports when completed should be placed before the

		committee for consideration of proposal for approval of the drug.
5	**Prasugrel Hydrochloride+Rosuvastatin**	The applicant did not turn up for presentation. Committee decided for discussing the proposal in the next meeting.
6	**Atenolol+Hydrochlorothiazide+Ramipril+** **Simvastatin**	The combination is proposed to be intended for secondary prevention of coronary heart disease in patients with multiple risk factors who have intolerance to aspirin or who are using aspirin for some other indication. Committee opined that such combination without aspirin cannot be considered for secondary prevention of coronary heart disease as aspirin is one of the most important component for such prevention. Therefore committee did not consider the proposed FDC as rationale for secondary prevention of coronary heart disease and did not recommend forgiving permission to market the proposed FDC.
7	**Prasugrel Hydrochloride +Aspirin**	Committee opined that both Prasugrel and Aspirin are used concomitantly in many patients for one year after Percutaneous coronary intervention (PCI). The firm conducted comparative clinical trial of Prasugrel versus clopidogrel as part of registration of Prasugrel where both the arms were given aspirin. Committee in principle recommended for approval of the FDC of Prasugrel 10mg + Aspirin 75/150mg only. However before formal approval, the firm should conduct the proposed BE study and report should be submitted to DCG(I) for consideration and giving final approval of the FDC by DCG(I).
8	**Multibic potassium free**	Recommended for giving permission to market the proposed FDC subject to condition that the formulation should be tested at IPC before launching the product in the market.
9	**Varenicline Tartrate**	The proposed study is to evaluate varenicline in smoking cessation in patients with post acute coronary syndrome. Committee opined that there is no need for conducting the proposed study in its present form and at present time in Indian context. Therefore committee did not recommend for

		giving permission to conduct the study.
10	**Simvastatin+Atenolol+ Ramipril+Hydrochlorothiazide+Aspirin+ Vitamin D**	Committee recommended for giving permission to conduct the study subject to condition that 50% of the trial sites should be multispecialty hospitals and Ethics Committee should be from the same area where the site is located.
11	**Cangrelor**	Committee recommended for giving permission to conduct the study. Committee opined that the proposed age limit in the study is justified.
12	**Dalcetrapib (R04607381)**	In this study placebo will be used on top of background standard care of therapy. Committee recommended for giving permission to conduct the study. Committee opined that the proposed age limit in the study is justified.
13	**MK-6621**	Committee recommended for giving permission to conduct the study subject to condition that patients with ejection fraction < 35% should be excluded from the study.
14	**AMR101**	Committee recommended for giving permission to conduct the study. Committee opined that the proposed age limit in the study is justified.
15	**Vanoxerine**	Committee opined that atrial fibrillation is a global issue and not an India specific issue and there is very inadequate Phase I/II clinical trial data specifically with respect to QT problem. The proposed study is also planned to be conducted only in India. The applicant may submit data/clarification addressing the above issues which may be placed before the committee for further consideration.
16	**Belatacept**	Committee recommended for giving permission to market the drug. In addition the firm will also clarify all relevant details of batches under stability studies such as batch size, scale, manufacturing date, expiry date etc. duly signed and certified.
17	**Darbepoetin alfa**	Committee recommended for giving permission to conduct the clinical trial. Report of the clinical trial when completed should be placed before the committee for consideration of proposal for approval of the drug.
Misc 1	**Ticagrelor**	The firm has submitted data of safety margin. Issue of higher bioavailability in Indian subjects was placed before the committee. Committee recommended for giving permission to market the drug.
Misc 2	**Safety changes in labelling for**	Committee agreed the line of action as taken

	some cholesterol lowering drugs known as statins on the lines of US FDA.	by USFDA and recommended for taking similar action in India.
Misc 3	**Number of subjects to be allowed from India in a global clinical trial.**	Committee discussed the issue and it will be deliberated further.

3. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 31.08.2012:-

The NDAC (Cardiovascular and Renal) deliberated the proposals on 31.08.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG	RECOMMENDATIONS
1	**Perflutren Lipid Microsphere Injectable**	The Phase IV study is proposed to be conducted to generate more safety data to meet the requirements of Post Marketing surveillance study as per the condition of Import permission issued to the firm for the drug. Committee recommended for the proposed Phase IV trial subject to condition that one more site preferably in Govt. Medical College/Hospital from eastern part of the country should be added and total number of subjects should be 280 in four sites.
2	**Choline fenofibarte 45mg and 135mg delayed release capsule**	Delayed release capsule containing choline fenofibarte, equivalent to 45mg/135mg of fenofibric acid is approved by USFDA. M/s Intas Pharma, has conducted open label, multicentric, randomized, clinical trial of Choline fenofibrate delayed release capsule in comparison of micronized fenofibate 160mg tablet in 226 patients of mixed dylipidemia having 12 week duration of treatment at 10 study centers. M/s Cadila Healthcare has also conducted comparative, multicentric, study to assess the efficacy and safety of choline fenofibrate delayed release capsules versus fenofibrate tablet in 222 subjects with dyslipidemia having 12 weeks duration of study. The committee examined the data and recommended for giving manufacturing and marketing permission to delayed release capsule containing choline fenofibarte, equivalent to 45mg/135mg of fenofibric acid for treatment of mixed lipidemia in combination with statins, severe hypertriglyceridemia.
3		Dipyridamole tablet is available in the country since long time. Dipyridamole

	Dipyridamole Injection **5 mg/ml**	Injection 5 mg/ml is marketed in USA, Canada and UK. The firm has submitted sub-acute toxicity study data. The firm has asked for waiver of clinical trial for marketing authorization. Justification furnished by the firm for asking waiver is that there are many published clinical trials in humans and there are already trials conducted in Asian patients so there wouldn't be need to conduct trial in Indian population. However there is no safety data on Indian population. The drug is for diagnostic purpose. Therefore the committee recommended that clinical trial is required to be conducted on at least 100 subjects in sites geographically distributed in the country. Accordingly protocol etc. should be submitted to DCG(I) for his approval. Clinical trial data so generated should be placed before the committee for consideration.
4	**Nicoumalone Tablets** **0.5/5/6 mg**	The committee noted that the proposed additional strengthsof 0.5mg/5mg/6mg of Nicoumalone Tablets will give better compliance and also help in fine titration. Hence the committee recommended for the grant of permission to manufacture and market the drug.
5	**Sildenafil Injection** **10 mg/12.5ml**	Sildenafil is a well established drug for Pulmonary Arterial Hypertension which is a life threatening and rare indication. Sildenafil Injection 10mg/12.5ml is approved and marketed in US.Sildenafil i.v. injection will be used only in acute condition. Therefore the committee recommended for giving permission to manufacture and market Sildenafil i.v. injection 10 mg/12.5ml without local clinical trial. However, phase IV clinical trial on 25 patients (considering the rare indication) should be conducted in Indian patients after getting protocol etc approved from DCG(I).
6	**Rivaroxaban** **15/20 mg Tablet**	Committee recommended that detailed India specific subset analysis of clinical trial data should be presented before the committee in

		the next meeting.
7	**Gadopentetic Acid Dimeglumine salt**	Committee opined that opinion of five radiologists should be obtained on the proposal and also on the requirement of local clinical trial for consideration of the committee.
8	**ClopidogrelBisulphate Tablets 75 mg**	There is no clinical data on Indian patients in support of use of ClopidogrelBisulphate Tablets 75 mg in atrial fibrillation. Committee recommended that clinical trial should be conducted in Indian patients. Accordingly clinical trial protocol etc. should be submitted to DCG(I) for approval. The data so generated should be placed before the committee for examination.
9	**Pitavastatin Calcium Tablet 4 mg**	The 4mg strength of Pitavastatin Calcium is approved in many countries including USA and there is no safety issue also. Accordingly committee recommended for the approval of Pitavastatin Calcium 4 mgtabletas additional strength.
10	**Tacrolimus Capsules 0.25 mg**	Tacrolimus 0.25mg is required for many patients. Hence committee recommended for giving permission to 0.25 mg tacrolimus as additional strength.
11	**Atorvastatin+ S(-)Metoprolol Succinate (ER) + Ramipril**	The firm presented clinical trial data generated in Indian patients. The committee opined that the data generated is not adequate for approval of the FDC. Hence the committee did not recommend for the approval of the FDC.
12	**Metoprolol Succinate (ER) + Ramipril**	Committee noted that there is no clinical data on this FDC for the proposed indication-Coronary Artery Disease.In absence of clinical data committee did not consider it rationale and did not recommend for its approval for the said indication.
13	**Atorvastatin Calcium + Fenofibrate**	Committee recommended that clinical trial is required to be conducted to access the percentage of patients who require the higher strength of Atorvastatin Calcium 20mg+ Fenofibrate 145mg as well as safety

		of the combination. Accordingly protocol etc should be submit to the office of DGC(I) for approval.
14	**Amlodipine+ Chlorthalidone+ Telmisartan**	As per the proposed protocol the study is planned to compare the efficacy of three drugAmlodipine, Chlorthalidone and Telmisartan vs Telmisartan and Amlodipine. The committee opined the proposed design is not addressing the rationality of FDC.
15	**Atorvastatin Calcium + Clopidogrel Bisulphate**	Committee opined that majority of patients do not require concomitant use of Atorvastatin Calcium and Clopidogrel Bisulphate. There is possibility of misuse of this combination. The data submitted in support of the use of this combination is also not adequate. Therefore committee did not recommend for approval of this combination.
16	**Bosentan**	The firm has informed that the sponsor Actelion Pharmaceuticals Ltd is working on major changes in the protocol including primary endpoint. They have put on hold the proposal globally till the protocol is finalized. Accordingly the proposal was deferred to be discussed in next meeting.
17	**Bosentan**	The firm has informed that the sponsor Actelion Pharmaceuticals Ltd is working on major changes in the protocol including primary endpoint. They have put on hold the proposal globally till the protocol is finalized. Accordingly the proposal was deferred to be discussed in next meeting.
18	**Mipomersen**	The committee recommended for giving approval for the global clinical trial subject to condition that upper age limit of the patients should be 65 years.
19	**PEG EPO**	Committee recommended the study subject to the following conditions. 1. The Inclusion criteria should be upto 60 years. 2. The phase II study in patients population can only be initiated after satisfactory evaluation of phase I study in healthy

		subjects by the DCG(I).

4. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 23.11.2012:-

The NDAC (Cardiology and Renal) deliberated the proposals on 23.11.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG	RECOMMENDATIONS
1	**Ibutilide Fumerate**	The drug is approved and marketed in USA since year 1995. It is indicated for the acute cardioversion of atrial fibrillation and flutter for which currently there is no satisfactory therapy. Hence committee recommended for giving permission for conducting the proposed clinical trial.
2	**Azilsartan Medoxomil 40mg/80mg tablets**	Earlier M/s. MSN submitted protocol for two arm comparative clinical trial. However the firm presented before the committee for 3 arm comparative study of Azilsartan 40mg vis a vis Azilsartan 80mg vis a vis Telmisartan. Committee recommended for giving permission to conduct the proposed clinical trial subject to the following conditions:- i) The inclusion criteria should be modified to include patients with mild to moderate hypertension only. ii) In a subset of 10% subjects, ambulatory BP should be measured pre and post. iii) The trial should be conducted in multispecialty hospitals including 50% Govt Hospitals/Institutes and the sites should be geographically distributed across the country. Protocol along with clinical trial sites as mentioned above should be submitted to DCG(I) for his approval and results of the trial should be placed before the committee for evaluation. In case of M/s Synokem, similar three arm comparative study of Azilsartan 40mg vis a vis Azilsartan 80mg vis a vis Olmesartan with similar conditions as above should be conducted.
3	**Telmisartan 40 mg + Rosuvastatin Calcium**	The firm presented the clinical trial data. Committee observed lot of discrepancies in the data especially in respect of primary efficacy

	10 mg Tablets	variable of LDL-C, SBP and DBP. Therefore committee did not recommend for approval of the FDC.
4	**Amlodipine + Indapamide Tablets**	Based on rationality, the committee recommended for approval of Indapamide 1.5mg SR + amlodipine 10mg strength of the FDC subject to condition that Phase IV clinical trial on 1000 patients with both Indapamide 1.5mg + Amlodipine 5mg/10mg should be conducted after getting protocol etc. approved by the office of DCG(I). As regards to the lower strength of indapamide 1.5mg + amlodipine 2.5mg, the committee felt that it is not essential, hence not recommended.
5	**Telmisartan 20 mg+ Amlodipine 2.5mg + HCTZ 6.25 mg**	Based on clinical data, the committee recommended for the approval of the proposed new strength of the FDC of Telmisartan 20 mg+ Amlodipine 2.5mg + HCTZ 6.25 mg in the country.
6	**Irbesartan 300mg+ HCTZ 12.5mg tablet**	Committee recommended for giving permission to manufacture & market the proposed new strength of the FDC of Irbesartan 300mg+ HCTZ 12.5mg tablet subject to the condition that single dose bioequivalence study should be conducted and its report alongwith comparative invitro dissolution data should be submitted to DCG(I) before approval of the FDC.
7	**S (-) Amlodipine + HCTZ + Olmesartan**	The firm presented the clinical trial data. The committee observed that the clinical trial data does not show significant benefit of the FDC over the comparator. Hence, committee did not recommend for the approval of the drug.
8	**Amlodipine + HCTZ + Losartan**	The clinical trial data generated in India for the proposed FDC was not considered adequate. Hence the committee did not recommend for approval.
9	**Rosuvastatin + Ramipril Capsules**	Committee recommended that a well designed phase 3 clinical trial demonstrating superiority in safety and efficacy of the combination of Rosuvastatin + Ramipril over Atorvastatin + Ramipril in statistically significant number of subjects is required to be conducted. Treatment duration of the trial should be at least 1 year. The

		trial sites should be multispeciality hospitals and 50% of the sites should be Govt. hospitals/Institutions. Protocol etc. should be submitted to DCG(I) for approval. Results of the trial should be placed before the committee for evaluation.
10	**Telmisartan + Chlorthalidone**	Committee recommended that a well designed phase 3 clinical trial demonstrating superiority in safety and efficacy of the combination of Telmisartan + Chlorthalidone over Telmisartan + Hydrochlorothiazide in statistically significant number of subjects is required to be conducted. Treatment duration of the trial should be at least 1 year. The trial sites should be multispeciality hospitals and 50% of the sites should be Govt. hospitals/Institutions. Protocol etc. should be submitted to DCG(I) for approval. Results of the trial should be placed before the committee for evaluation.
11	**Atorvastatin + Vitamin D3**	Committee recommended that a well designed phase 3 clinical trial demonstrating superiority in safety and efficacy of the combination of Atorvastatin + Vitamin D3 over Atorvastatin alone in statistically significant number of subjects is required to be conducted. Treatment duration of the trial should be at least 1 year. The trial sites should be multispeciality hospitals and 50% of the sites should be Govt. hospitals/Institutions. Protocol etc. should be submitted to DCG(I) for approval. Results of the trial should be placed before the committee for evaluation.
12	**Fibrinogen Concentrate (Human)**	Committee recommended for giving permission to conduct the study.
13	**CLOTINASE (Recombinant Human Staphylokinase Injection)**	The drug is not approved in any country. The trial data presented by the firm on 120 patients has shown 0% mortality and 68.3% TIMI-3 coronary flow which looks encouraging. However the data is not adequate to come to a conclusion that the drug is safe and effective and can be considered for marketing. Committee recommended for conducting a well designed clinical trial on 1000 patients. Protocol etc. for the trial should be submitted to DCG(I) for approval.

14	**PEG EPO (Pegylated Erythropoietin)**	Committee recommended for giving permission to conduct the study.
15	**Rivaroxaban tablets 10mg/15mg/20mg**	The firm presented India specific subset analysis of clinical trial data. Committee recommended for giving permission to market Rivaroxaban tablets 15mg and 20mg for the proposed indication.

5. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 02.03.2013:-

The NDAC (Cardiology and Renal) deliberated the proposals on 02.03.2013 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
Special agenda 1 to 7			
1	**EVEROLIMUS**		The Committee was apprised that the Parliamentary Standing Committee (PSC) for the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on 08.05.2012 on the functioning of the CDSCO. The report has made various recommendations and observation on various aspects such as approval of New Drugs, Pharmacovigilance, approval of clinical trials etc. The Ministry of Health & Family Welfare has submitted final action taken report on the observation/recommendations contained in the 59th report of the Hon'ble Parliamentary Standing Committee. As per the action taken report, it has been decided by the Ministry that 73 drugs including Fixed Dose Combinations, on approval of which the Hon'ble PSC has made various observations, would be referred to the NDACs for examination and review related to continued marketing of these drugs and updating of their product monographs in light of recent knowledge and regulatory changes overseas. Out of these 73 drugs, 7 drugs are in the category of Cardiology and Renal which are given below:- 1. EVEROLIMUS 2. MOXONIDINE 3. ALISKIREN 4. DRONEDARONE 5. LEVOSIMENDAN 6. AMBRISENTAN 7. ADEMETIONINE The NDAC (Cardiology and Renal) discussed the issue and noted that Ministry of Health & Family Welfare has already constituted a Committee to formulate policy guidelines and SOPs for a) approval of new drugs. clinical trials, and banning of drugs under the
2	**MOXONIDINE**		
3	**ALISKIREN**		
4	**DRONEDARONE**		
5	**LEVOSIMENDAN**		
6	**AMBRISENTAN**		
7	**ADEMETIONINE**		

			Chairmanship of Dr. Ranjit Roy Chaudhury and b) for approval of the Fixed Dose Combinations under the Chairmanship Dr. C.K. Kokate. Therefore, the Committee opined that the above five drugs related to continued marketing and updating of the product monograph in the light of recent knowledge and regulatory changes overseas could be examined as per policies, guidelines and SOPs being prepared by the Dr. Ranjit Roy Chaudhury Committee and Dr. C.K. Kokate Committee. However, in the meantime the data/information on safety, efficacy of these five drugs including published data, PMS/PSUR, PSUR data especially on Indian patient required to be prepared in the Form of Dossier. Such data should be prepared from three different sources viz. i) by CDSCO ii) by Pharmacovigilance Programme of India (PvPI) and iii) the firm concerned. The Dossier shall be circulated to all the experts of the NDAC(Cardiology and Renal) for their further review. If needed manufacturer may be requested to make their Presentation before the NDAC on safety and efficacy of the drugs. Committee also noted that out of the above seven drugs, ademetionine which is indicated for intra hepatic cholestasis and liver diseaseshould be referred to NDAC (Gastoenterology and Hepatology).
8	**Efonidipine HCl**		The Committee recommended for giving approval to the clinical trialand BE study subject to the following conditions:- **i)** The following should also be included in exclusion criteria:- **a)** Females with child bearing potential. **b)** Instead of severe congestive heart failure, all congestive heart failure patientsshould be mentioned. **ii)** Sample size rationale should be submitted. **iii)** Principal Investigator (PI) in the clinical trial site Indira Gandhi Medical Hospital, Nagpur should be mentioned as coordinator and the

			name of PI in that site should be mentioned. **iv)** Regarding compensation, Patient information sheet as per new notification along with the Sponsor Undertaking as per latest amendment should be submitted. Revised protocol incorporating the above changes should be evaluated by the committee.
9	**Edaravone 30mg Tablet**		The Committee opined that the firm should submit oral Pharmacokinetic data before considering the application for the proposed clinical trial. Committee also observed several deficiencies in the clinical trial protocol and advised to submit a revised comprehensive protocol.
10	**Aspirin+Clopidogrel +Rosuvastatin**		The Committee opined that there is no essentiality of the proposed fixed dose combination. Therefore committee did not recommend for giving permission to the proposal.
11	**Multibic potassium free**		The Committee opined that revised protocol should be submitted to the office of DCG(I) incorporating the following:- **i)** Incorporate clinical endpoints in the protocol. **ii)** Comparator should be the solution containing similar composition with reference to Potassium. **iii)** The sample size should be recalculated and justified. **iv)** The inclusion criteria should be revised to reduce the upper age limit to 60 years. **v)** Reasonable representation of sites from Govt. hospitals should be incorporated. **vi)** Regarding compensation, Patient information sheet as per new notification along with the Sponsor Undertaking as per latest amendment should be submitted. Revised protocol incorporating the above changes should be evaluated by the committee.
12	**Hydrochlorothiazide +**		The combination of the applied product is

	Telmisartan		already approved in India. The proposed higher strength is already approved in USA, Canada, Europe, Brazil etc. The Committee recommended for grant of manufacturing and marketing permission for the proposed FDC subject to post marketing surveillance.

6. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 21.03.2013:-

The NDAC (Cardiology and Renal) deliberated the proposals on 21.03.2013 and recommended the following:-

AGENDA	NAME OF DRUG	RECOMMENDATIONS

NO.		
1	**Dabigatran Etixilate**	Committee recommended that the drug can be sold by retail on prescription of neurologist also.
2	**Treprostinil Diethanolamine**	Committee recommended that the firm should submit detailed safety profile along with mortality data of the previous studies with the drug which would be evaluated by the committee.
3	**Treprostinil Diethanolamine**	Committee recommended that the firm should submit detailed safety profile along with mortality data of the previous studies with the drug which would be evaluated by the committee.
4	**Betrixan**	Proposed clinical trial is the first phase III clinical trial to compare extended duration Betrixaban with standard of careEnoxaparin for prevention of venous thromboembolism in acute medically ill patients. However safety, efficacy data presented was not found adequate to allow the first phase III clinical trial in medically sick patients. Hence Committee did not recommendfor giving permission for the study.
5	**Lathanum Carbonate**	The committee recommended for the conduct of clinical trial subject to following conditions. **1.** In India only part 2 and part 3 of the study should be conducted. **2.** Patients aged 12-18 years only should be included in the study. **3.** Study sites should be multispecialty hospitals/institutes. Study site Supreme Kidney Site, Nashik, Maharashtra should be excluded. Further Undertaking for providing compensation by the sponsor and ICD as per GSR 53 (E) dated 30.01.2013 should be submitted along with the above information to the DCG (I).
6	**Carvedilol**	Carvedilol CR tablet is already approved in India. Committee noted that proposed study is planned to be conducted for generating data for Brazilian Regulatory Authority and has no benefit on Indian populations. Hence the committee did not recommend for the study.
7	**Simvastatin+Amlodipine+Losartan+Hydrochlorothiazide**	The committee observed that the essentiality and desirability of the proposed FDC of Simvastatin+Amlodipine+Losartan+Hydrochlorothiazide is doubtful. Hence committee did not recommend for approval of the FDC.

8	**Sevelamer Carbonate 800 mg Tablets**	Sevelamer Carbonate tablet is already approved in India. Committee noted that proposed study is planned to be conducted in India for generating data for submission to foreign regulatory authority only and has no benefit on Indian populations. Hence the committee did not recommend for the study.
9	**ACT-293987 (Protocol Amendment)**	Committee recommended for approval of the proposed amendments except the local amendment which will a Right Heart Catheterization (RHC).
10	**Evacetrapib**	The committee recommend for giving permission to the trial. However the sites should be Multispecialty hospitals/institutes having own Institutional Ethics Committee including 50% of sites being government hospitals across the country. The list of such sites along with Undertaking etc from the Investigators should be submitted to DCG (I) for consideration and approval of the study. Further Undertaking for providing compensation by the sponsor and ICD as per GSR 53 (E) dated 30.01.2013 should be submitted along with the above information to the DCG (I).
11	**AMG 145**	The committee recommend for giving permission to the trial. However the sites should be Multispecialty hospitals/institutes having own Institutional Ethics Committee including 50% of sites being government hospitals across the country. The list of such sites along with Undertaking etc from the Investigators should be submitted to DCG (I) for consideration and approval of the study. Further Undertaking for providing compensation by the sponsor and ICD as per GSR 53 (E) dated 30.01.2013 should be submitted along with the above information to the DCG (I).
12	**SAR236553/REGN727**	The committee recommend for giving permission to the trial. However the sites should be Multispecialty hospitals/institutes having own Institutional Ethics Committee including 50% of sites being government hospitals across the country. The list of such sites along with Undertaking etc from the Investigators should be submitted to DCG (I) for consideration and approval of the study. Further Undertaking for providing compensation by the sponsor and ICD as per GSR 53 (E) dated 30.01.2013 should be submitted along with the above information to the DCG (I).
13	**SAR236553/REGN727**	The committee recommend for giving permission to the trial. However the sites should be Multispecialty

		hospitals/institutes having own Institutional Ethics Committee including 50% of sites being government hospitals across the country. The list of such sites along with Undertaking etc from the Investigators should be submitted to DCG (I) for consideration and approval of the study. Further Undertaking for providing compensation by the sponsor and ICD as per GSR 53 (E) dated 30.01.2013 should be submitted along with the above information to the DCG (I).
14	**Darbopoetin alfa (R-TPR-026)**	The committee recommend for giving permission to the trial in Anemia due to Chronic Kidney Disease subject to the following conditions- 1. The upper limit of the target Hemoglobin should be 11.5. 2. The sites should be Multispecialty hospitals/institutes having own Institutional Ethics Committee including 50% of sites being government hospitals across the country. The list of such sites along with Undertaking etc from the Investigators should be submitted to DCG (I) for consideration and approval of the study. Further Undertaking for providing compensation by the sponsor and ICD as per GSR 53 (E) dated 30.01.2013 should be submitted along with the above information to the DCG (I).
15	**Abciximab**	Committee noted that as per the result of the clinical trial presented, there was zero % mortality and morbidity which is unusual in such cases. Committee recommended for approval of the product subject to condition that the firm should generate post marketing surveillance data including 30 day mortality on 1000 patients within 1 year and submit the same to the committee for review of the manufacturing permission for continued marketing of the product.
16	**Rituximab**	The proposal was deferred as Dr. Arvind Bagga could not come for presentation to the committee.

7. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 18.06.2013:-

The NDAC (Cardiology and Renal) deliberated the proposals on 18.06.2013 and recommended the following:-

S.NO	DRUG NAME	RECOMMENDATION
1.	**Ambrisentan+Tadalafil**	Both Ambrisentan & Tadalafil are approved for pulmonary arterial hypertension. Committee recommended for the proposed clinical trial.
2.	**Cicletanine**	The Committee recommended that a comparative clinical trial of Cicletanine V/s. chlorothalidone

		should be carried out on atleast 600 patients with one year treatment duration. The patients with BMI≥30kg/m² as well as with patients with low dose of aspirin should not be excluded from the study. The Firm should submit the revised clinical trial protocol along with details of sites which should be multispecialty hospitals/medical colleges having emergency facilities and geographically distributed in the country along with status of EC registration.
3.	**Rituximab**	The applicant was absent and no communication has been received. Hence ,the proposal was deferred.
4.	**(Antihemophilic factor VIII) Application for grant of permission to import and market Green Gene Lyophilized powder and solution for injection (Antihemophilic factor VIII)500 IU/10 ml Vial from green cross corporation,korea**	The applicant was absent and no communication has been received. Hence ,the proposal was deferred.
5.	**Lanthanum Carbonate suspension 250 mg/ml**	The committee recommended conducting of phase III Clinical trial of Lanthanum Carbonate suspension V/s. Lanthanum Carbonate tablet and CT protocol shall be submitted to committee for evaluation.
6.	**Nifedipine ER Tablet 60 mg**	Nifedipine ER Tablet is already approved in the country since long time back. The committee recommended for giving permission of bioequivalence study as per the protocol submitted by the firm.
7.	**Indapamide +peridopril Erbumin**	The committee opined that the proposed higher strength of the FDC may be useful. However before taking final decision, the firm should submit the clinical data including published data in support of the product. Further the firm should also submit the justification for not conducting bioequivalence study. These information/data should be submitted to the committee for examination.
8.	**Choline Fenofibrate DR+Rosuvastatin IR**	The committee opined that both the drugs are used concomitantly.The firm also presented the supportive clinical data in support of the FDC. The committee recommended that firm should submit revised CT protocol to DCG(I) .However the committee recommended for proposed BE Study and submit BE study report for further consideration.
9.	**Ezetimibe +Rosuvastatin Calcium**	The combination of Ezetimide 10mg/10mg+Rosuvastatin 5mg/10mg is already approved. The committee opined that Rosuvastatin are used concomitantly with Ezetimide 10mg.The firm has also submitted the published report of clinical trial in support of the proposed strength.Similar FDC of simvastatin 20 mg/40mg with Ezetimide 10 mg. Approved by US FDA.The

		committee recommended for giving permission for conducting BE Study and accordingly firm should submit the BE study report for further consideration.
10.	**Edaravone Tablets 30mg**	The committee recommended for presentation of clinical trial protocol and pharmacokinetic protocol together with clear objective and aim of proposal.
11.	**Azelnidipine 8mg/16mg tablet**	The committee recommended for the approval of the phase III Clinical trial subject to the following conditions: • The comparative drug should be Amlodipine 10 mg. • Trial should be conducted in 600 patients for a period not less than one year. • The sites should be geographically distributed in multispeciality hospitals with emergency care facilities and having institutional ethics committee. Revised protocol etc. as above should be submitted to DCG(I) for his approval. Report of the study along with BE study report should be submitted for further consideration.
12.	**Losartan potassium 50mg+Amlodipine 5mg+Hydrochlorothiazide 12.5 mg tablet**	The committee considered the proposed clinical trial, however the committee recommended for conducting the clinical trial with a treatment period of 12 months and the number of subjects shall be statistically significant. The report of the clinical trial shall be submitted to the committee for further evaluation.

8. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 24.08.2013:-

The NDAC (Cardiology and Renal) deliberated the proposals on 24.08.2013 and recommended the following:-

Agenda no.	File no	Recommendations
1	**(Rituximab)** **Study the efficacy of early Rituximab administration in**	The applicant did not turn up. Hence proposal has been deferred.

	maintaining remission in steroid sensitive	
2	**Ticagrelor Tablets**	The firm presented the overall safety data and PSUR data before the committee. Considering these data committee recommended that the drug may be allowed to be sold by retail on the prescription of cardiologist and internal medicine specialities.
3	**Efonipidine**	Earlier NDAC committee recommended for giving approval to the clinical trial and BE study subject to the following conditions:- i)The following should be included in exclusion criteria:- a) Female with child bearing potential b) Instead of severe congestive heart failure, all congestive heart failure patients should be mentioned. ii) Sample size rational should be submitted. iii) Principle investigator (PI) in the clinical trial site Indira Gandhi medial Hospital, Nagpur should be mentioned as co-ordinator and the name of (PI) in that site should be mentioned. iv)Regarding compensation, Patient information sheet as per new notification along with the Sponsor undertaking as per latest amendments should be submitted. Revised protocol incorporating the above changes should be evaluated by the committee. The firm presented the sample size justification along with the details of sites etc. Considering this the committee recommended for the approval of the study.
4	**Rivaroxaban**	The firm presented data on one indication only. The committee recommended that detailed data including data of all clinical trials conducted in India should be presented before the committee.
5	**Cilnidipine 20mg Tablet**	The committee recommended for the grant of permission to conduct BE study. The firm should submit BE study report with PMS data/PSUR of marketed product for evaluation by the committee.
6	**Amlodipine Orally Disintegrating Strips**	The formulation of Amlodipine Orally Disintegrating Strips is a new formulation not approved in any country. The firm has requested for wavier of clinical trial which was not accepted by the committee. It was recommended that the proposal of the firm to manufacture and market Amlodipine Orally Disintegrating Strips cannot be considered.

7	**Apixaban 2.5/5mg tablets**	The firm presented the result of global clinical trial (ARISTOTLE) conducted globally in more than 18,000 patients, which had 600 patients from India. The proposed new indication is approved by USFDA, EMA. The firm also presented an ongoing clinical trial (LTOLE) in which it was shown that 28 patients out of 125 patients from India was lost to follow-up. The committee recommended that the firm should submit following for further consideration. i) Details of the 28 patients lost to follow-up in (LTOLE) study. ii) Plan to conduct PMS (Phase IV) clinical trial in India.
8	**S (-) Amlodipine Besylate IP + Hydrochlorothiazide IP + Olmesartan Medoxomil**	The three drug consideration was considered in previous meeting and was not approved because of lack of sufficient benefits of proposed FDC over comparator. The applicant presented the following:- Advantage of S (-) Amlodipine over Amlodipine is that the equi-effective dose of S (-) Amlodipine is half that of Amlodipine. Incidences of Pedal oedema with S (-) Amlodipine is reported to be significantly less than that of Amlodipine. Detailed data of CT conducted in India showed non-inferiority. Since the equi-effective dose of S (-) Amlodipine in combination of S (-) Amlodipine Besylate IP + Hydrochlorothiazide IP + Olmesartan Medoxomil is half of Amlodipine in combination of Amlodipine Besylate IP + Hydrochlorothiazide IP + Olmesartan Medoxomil which is already approved in India as well as US, the committee recommended for approval of the FDC subjected to the condition that the firm should have intense PMS and submit data regularly.
9	**Prasugrel Hydrochloride+ Aspirin**	The proposal of Aspirin + Prasugrel Hydrochloride capsule was earlier deliberated by the NDAC (Cardiology and Renal) meeting on dated: 21.04.2012 wherein committee had recommended that both Prasugrel and Aspirin are used concomitantly in patients for Percutaneous coronary intervention (PCI). Committee in principle recommended for approval of the FDC. However before formal approval the firm should conduct the proposed BE study and report should be submitted to DCG(I) for consideration and giving final approval of the FDC by DCG(I). The permission however was not granted as the matter was to be re-examined with NDAC for the requirements

		of clinical trial. After detailed deliberation, committee opined that Prasugrel is used concomitantly with aspirin in clinical practice for aforesaid indication. Further FDC of Prasugrel Hydrochloride+ Aspirin will improve the patient compliance. BE study as presented by the firm has shown that test product is bioequivalent to reference product. In view of this further clinical trial was not considered necessary by the committee. Committee recommended for the approval of FDC of Prasugrel Hydrochloride 10 mg + Aspirin 75 mg for Percutaneous Coronary Intervention (PCI) subjected to condition firm should have intense PMS for the FDC.
10	**Telmisartan + Chlorthalidone**	After detailed deliberation the committee recommended for clinical trial with treatment duration of 6 months. Accordingly firm should submit the revised protocol to the office of DCG (I) for approval and results of the study shall be submitted to the committee before approval for manufacturing and marketing.
11	**SAR236553**	The committee recommended granting of permission for conduct of clinical trial with the condition that sites should be multispecialty hospital/ Government medical college with emergency facility and institutional ethics committee duly registered with office of DCG (I).
12	**Observation study**	The committee was informed about the definition of clinical trial under Rules 122DAA of Drug and Cosmetic Rules 1945 as follows: Rules 122DAA- Definition of clinical trial: For the purpose of this part, “Clinical trial” means a systemic study of new drug(s) in human subjects(s) to generate data for discovering and/or verifying the clinical pharmacological (including pharmacodynamic and pharmacokinetic) and/or adverse effects with the objective of determining safety and/or efficacy of the new drug. The study presented by firm does not involve use of any new drug(s). Therefore, the proposed study does not come under the aforesaid definition of clinical trial under Rule 122DAA of Drug & Cosmetic Rules. Committee agreed for the same.
13	**Treprostinil Diethanolamine (Protocol No. TDE-PH-310)**	The firm has failed to present complete safety data of earlier studies 302 & 304 conducted in India. Therefore the committee recommended that the applicant should present the complete safety data before the committee in its next meeting.
14	**Treprostinil Diethanolamine**	The firm has failed to present complete safety data of earlier studies 302 & 304 conducted in India. Therefore the committee recommended that the applicant should

	(Protocol No. **TDE-PH-311)**	present the complete safety data before the committee in its next meeting.
15	**(Antihemophilic factor VIII)** **Application for grant of permission to import and market GreenGene Lyophilized powder and Solution for injection (Antihemophilic Factor VIII) 500 IU/10 ml Vial from Green Cross Corporation, Korea**	Withdrawn by the firm
16	**Darbepoetin alfa**	Proposal was deferred for next meeting.
17	**Darbepoetin alfa**	Proposal was deferred for next meeting.
18	**Darbepoetin alfa**	Proposal was deferred for next meeting.

9. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 27.09.2013:-

The NDAC (Cardiology and Renal) deliberated the proposals on 27.09.2013 and recommended the following:-

Agenda no.	Name of the Drug	Recommendations
1	**Canrenone**	Firm made presentation before the committee for conducting the clinical trial with Canrenone in the treatment of Stage I hypertension. After deliberation the committee noted that the proposed drug aldosterone antagonist is not approved internationally for management of essential hypertension. The committee did not agree for the conduct of study in present form.
2	**Dabigatran Etexilate**	Committee noted that firm does not have Indian subset analysis data of 126 subjects enrolled in the study no. 1160.71 study name “RELY-ABLE”. The firm has

		proposed to conduct observational, non-interventional study in India as a part global study. After deliberation the committee recommend that firm should submit initially the Indian subset analysis data of study no. 1160.71 study name “RELY-ABLE” before the committee. Further action on conducting phase IV clinical trial will be taken accordingly.
3	**Everolimus**	Committee noted that certain ethical aspects are not addressed properly by the firm. The committee recommended that firm should address the following ethics concerns for further review by the committee: i) Status of graft deterioration during the study. ii) Continuation of the drug to the trial subjects after completion of the study as the drug is to be used for lifelong.
4	**Ivabradine Hydrochloride 5mg/7.5mg Tablet**	Based on the global clinical trial data in which India was also the part of global clinical trial, committee recommended for grant of permission for additional indication for Ivabradine Hydrochloride 5mg/7.5mg Tablet.
5	**Hydrochlorothiazide CR Tablet 12.5mg (Protocol Amendment)**	The committee recommended the approval of proposed amendments in clinical trial protocol.
6	**UT-15C** **Protocol Number-TDE-PH-310**	Based on the clarification now presented on the safety profile of the drug in Indian subjects vis a vis global subjects (during the other trials with this drug) the committee recommended that the present protocol TDE-PH-310 trial can be conducted. The sites should be multispecialty sites having emergency facilities & Registered Ethics Committees. 50% sites should be in govt. Medical college
7	**UT-15C** **Protocol Number- TDE-PH-311**	Based on the clarification now presented on the safety profile of the drug in Indian subjects vis a vis global subjects (during the other trials with this drug) the committee recommended that the present protocol TDE-PH-311 trial can be conducted. The sites should be multispecialty sites having emergency facilities & registered Registered Ethics Committees. 50% sites should be in govt. Medical college
8	**Losartan Potassium 50 mg + Amlodipine 5mg + Hydrochlorthiazide 12.5 mg tablets**	The firm presented the international guidelines about efficacy as well as maintenance parameters for duration of 6 months study. Although the firm proposed duration of 3 months study, however the committee recommended for 6 months study to assess safety and efficacy parameters.

9	**Atorvastatin Calcium 10/20 mg + Vitamin D3 1000 IU/1000 IU tablet**	The firm presented the international guidelines about efficacy as well as maintenance parameters for duration of 6 months study. Although the firm proposed duration of 3 months study, however the committee recommended for 6 months study to assess safety and efficacy parameters.
10	**Multiple Potassium Free 2mmol/l & 4mmol/l**	The committee observed that the firm has incorporated all the points/ suggestions suggested by the committee in its meeting held on 02.03.2013. Accordingly the committee recommended for approval of proposed phase III clinical trial.
11	**Darbepoetin alfa (additional route of administration i.e. Intravenous)**	The committee observed that the change of route of administration attracts the definition of a subsequent new drug approval. Therefore the firm may be asked to conduct the study using IV route in not less than 100 CKD patients of 12 weeks therapy.
12	**Darbepoetin alfa**	The committee asked the firm to make presentation of the entire data in the next NDAC meeting.
13	**Darbepoetin alfa**	The committee observed that the PMS data is found to be satisfactory.
14	**Abciximab**	The committee recommended for the PMS study protocol as proposed by the firm.

10. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 29.10.2013:-

The NDAC (Cardiology and Renal) deliberated the proposals on 29.10.2013 and recommended the following:-

Agenda no.	Name of the drug	Recommendations
1	**Ambrisentan and Tadalafil**	The proposal was deliberated earlier in NDAC (Cardiology and Renal) held on 18/06/2013, where only two experts were present. However, the Technical Committee in its meeting held on 25/07/2013 has recommended that the proposal recommended by only two experts of NDAC shall be further deliberated by concerned NDAC with a proper representation of member during the meeting, The proposal again deliberated the NDAC and the committee recommended for conducting proposed study

2	**Fenoldopam Mesylate 10mg/1ml & 20mg/2ml injection**	The firm has proposed to manufacture and market Fenoldopam Mesylate 10mg/1ml & 20mg/2ml Injection, to be indicated for the in-hospital, short-term (up to 48 hours) management of severe hypertension which is a life threatening condition and firm requested for waiver of conducting local clinical trial. The Committee noted that the drug is approved in USA since 1997 and recommended that Phase-III clinical trial is required to be conducted on Indian patients as alternative drugs are already available in the country. Accordingly, protocol etc. should be submitted before the Committee for further taking necessary action in the matter.
3	**Azelnidipine Tab. 8mg / 16mg**	The Committee was informed that the committee in its meeting held on 21.04.2012, had recommended that comparative non inferiority clinical trial of Azelinidipine vs Amlodipine 10mg OD in statistically significant number of subjects should be conducted. Further, the committee also deliberated in a similar case of another firm wherein, the committee in its meeting held on 18.06.13 recommended to conduct comparative clinical trial with amlodipine 10mg in 600 patients for a period of not less than one year. After deliberation the Committee recommended for the conduct of clinical trial as per the protocol submitted having six months duration of treatment.
4	**Apixaban 2.5/5mg**	The firm presented data of 23 subjects who discontinued the Apixaban drug the LTOLE (out of 125 subject who enrolled in the trial from India) after examining these data and regulatory status of proposed indication is approved in USA and various European countries the committee recommended for grant for additional indication Apixaban 2.5/5mg tab. for"Prevention of stroke and systemic embolism in adult patients with non-valvular atrial-fibrillation (NVAF), including those with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); >75 years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class >II).Compared to warfarin, Eliquis also results in less bleeding, including intracranial hemorrhage." The committee also recommended for phase IV clinical trial waiver based on global clinical trial where in India is also participating country (A total of 804 patients were randomised from India) and firm is already conducting phase IV study for different indication in India.

5	**Cilnidipine Tablets 20mg**	The firm has stated that the proposed drug Cilnidipine Tablets 20mg has approved in Japan the committee recommended for grant of BE study of the proposed drug with the condition that the reference drug should be Innovator product.
6	**Clinidipine 10mg +Telmisartan IP 40mg**	Committee opined that the firm failed to present that FDC has any added advantage over the two drugs used separately other than the compliance. Further the proposed FDC is not approved anywhere in the world and there would be difficult for the physician in dose trituration with the FDC. Hence the committee did not recommend the FDC.
7	**Belimumab**	The committee opined that the trial be conducted only at multispecialty/superspeciality hospitals with emergency care facility. 50% of the sites shall be at government hospitals. The revised list of site's has to be submitted for final opinion by the NDAC.
8	**Sevelamer hydrochloride**	The firm has withdrawn the proposal.
9	**Carvedilol CR**	The committee opined that study sponsored by M/s Libbs Farmaceutica, Brazil (a Brazilian company). The proposal of conduct of clinical trial to fulfil the regulatory requirement of Brazillian Regulatory Authority. Apparently, there is no benefit to Indian population for proposed clinical trial , hence the committee has rejected the proposal to conduct the clinical trial.
10	**Darbepoetin alfa 25 mcg/0.42 ml, 40 mcg/0.4ml, 60mcg/0.3ml, 100 mcg/0.5 ml, 150 mcg/0.3 ml, 200 mcg/0.4ml, 300mcg/0.6ml & 500 mcg/1ml Prefilled Syringe**	Firm presented the efficacy and safety data (clinical trial data) of their indigenously developed drug Darbepoetin alfa for subcutaneous use. It was observed that 17 SAEs occurred during the Phase III clinical trial. Therefore firm is required to submit the baseline data of all the 17 patients on which SAEs were observed. **The committee recommended for grant of manufacture & marketing of Darbepoetin alfa injection prefilled syringe for SC route subject to the approval of baseline data by the experts of NDAC.** Further committee recommended that Marketing authorization at this stage shall only be considered for subcutaneous route. As the clinical study was not done wit, Intravenous route.,this rout was not considered. Firm shall also include report on immunogenicity study in their PSURs regularly.
11	**3/KD/8/7/Reliance/Albumin/13 -BD**	The committee deliberated on the request of company to include other six indications. All these indication are subtype of already mentioned indication i.e. hypervolemia, hypoalbunemia and hypoprotienemia.

		The committee was also informed that several other overseas manufacture having approved package insert which mentioned indication in similar manner as requested by the firm. The committee asked CDSCO to check the original approved package insert and present in next meeting in order to harmonise the indication.

11. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 12.12.2013:-

The NDAC (Cardiology and Renal) deliberated the proposals on 12.12.2013 and recommended the following:-

AGENDA NO.	Name of the Drug	RECOMMENDATIONS
1.	**Rivaroxaban)**	The committee was informed that the Parliamentary Standing Committee (PSC) of the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on the functioning of CDSCO. The committee had made various recommendations and observations on approval of certain new drugs. Rivaroxaban is one of such drug. This Directorate had approved the Rivaroxaban 10 mg (Tablet) for prevention of venous thromboembolism (VTE) in adult patients undergoing hip or knee replacement surgery on 03rd Feb. 2010. As per action taken report, it was decided that the drug would be referred to NDAC for examination and review the issue related to continue marketing of the drug and updating of the product monograph in light of recent knowledge & regulatory changes overseas. Earlier this proposal was deliberated in NDAC meeting held on 24.08.2013. The Committee recommended that

		detailed data including data of all clinical trials conducted in India should be presented before the Committee. Accordingly, the firm presented detailed data including that of RECORD -2 and RECORD -4 clinical trials which were conducted in India as part of global clinical trial, along with PMS Data generated in India as well as abroad. The drug is currently marketed in 130 countries and there is no restriction /suspension on the use of the drug in any country. Considering all the above aspects, the Committee recommended that marketing of the drug should continue for the indication already approved in the country. No change in package insert is required at present.
2.	**Dronedarone**	The committee was informed that Parliamentary Standing Committee (PSC) of the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on the functioning of CDSCO. The report had made various recommendations and observations on approval of certain new drugs. Dronedarone Hydrochloride is one of such drug. The drug dronedarone hydrochloride 400mg (Tablet) was approved to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistant atrial fibrillation (AF) or artial flutter (AFL), With a recent episode of AF/AFL and associated, cardiovascular risk factors (i.e., age >70, Hypertension, Diabetes, prior cerebrovascular accident, left atrial diameter > 50mm or left ventricular ejection fraction (LVEF) < 40%), who are in sinus rhythm or who will be cardioverted. As per action taken report, it was decided that the drug would be referred to NDAC for examination and review the issue related to continue marketing of the drug and updating of the product monograph in light of recent knowledge & regulatory changes overseas. Accordingly, detailed dossier on the drug was already forwarded to the Committee members. The firm presented detailed data on safety and efficacy of the drug. The drug was approved based on the ATHENA clinical trial which was a global clinical trial in which India was a participating country with 21 patients. After the approval of the drug, the firm was permitted to conduct another global study. However, the same could not be initiated by the firm due to less recruitment of patients in India. The drug is currently marketed in more than 73 countries including USA and EU. Presently the firm is also not actively promoting the marketing the drug. The firm should submit the same in writing to DGCI. Since no other safer drug is available for the approved indication, the Committee recommended that the marketing of the drug should continue with the precautions, warning etc as reflected in the package

		insert.
3.	**Hydroxychloroquine sulphate tablet 200/400mg**	The committee recommended for the study, with the condition to. 1. Modify inclusion criteria : Renal insufficiency to moderate instead of moderate to severe 2. Ultra sound to be carried out to rule out renal artery stenosis 3. Modify exclusion criteria: Abnormal renal function/Renal failure to be removed and change hyper parathyroidism to Primary hyper parathyroidism. 4. BUN, Serum creatinine and Serum electrolytes should be done on each visit. Accordingly revised protocol should be submitted to the O/o of DCG(I) for necessary action.
4.	**Azilsartanmedoxomil+Chlorthalidone**	Azilsartan drug is yet to be approved for manufacturing and marketing in the country. Committee opined that proposal will be considered for conducting clinical trial once DCG (I) office issues approval for conducting clinical trial for Azilsartan drug.
5.	**Chlorthalidone+ Olmesartan Medoxomil**	The design of the study proposed by the firm was not found satisfactory as superiority of test product cannot be proved as per the study design. Firm should revise the protocol and shall be placed again before the committee for further consideration.

6.	**Everolimus**	The firm has applied for the grant of permission to conduct a phase IV. The trial drug Everolimus(RAD001), is a macrolide immunosuppressant and is being further investigated in de novo renal transplantation. Everolimus is already in India w.e.f. dated 4 Sep 2004.The proposed study is planned to be conducted in 10 countries including Canada, USA and India and the same is already approved in Germany & Spain. Out of Globally proposed 2040 patients, in INDIA 150 multi-organ transplant recipients patients will be studied. This is a 2-year, randomized, open label, 2-arms study evaluating graft function with Everolimus with reduced exposure CNI, compared to Mycophenolc acid with standard exposure CNI. The committee deliberated the proposal and opined that the study can be conducted with a condition that the Informed consent form shall include the following: the study drug will be provided to the trial participant only for the treatment duration and after the trial is concluded the subjects have to bear the cost by themselves.
7.	**Erythropoetin**	The committee approved the PMS results.
8.	**Darbepoeitin alfa**	The committee approved the baseline data of all 17 patients on which SAEs were observed and recommended the approval of drug for marketing authorization as per earlier decision in the NDAC meeting held on 29/10/2013. It is also recommended that the drug will be sold under the prescription by RMP.

12. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 24.01.2014:-

The NDAC (Cardiology and Renal) deliberated the proposals on 24.01.2014 and recommended the following:-

Agenda no.	Name of the Drug	Recommendations

1.	**Bivalirudin**	The drug was approved in India as an anti-coagulant in treatment of PCTA on 25-8-2005. The applicant presented the published clinical trial reports of Bivaluridine Injection in pediatric population. After deliberation, the Committee recommended for approval of the proposed trial subject to the following:- 1. Patients of age limit 1-12 years shall be included 2. Infants shall be excluded. 3. The total number of subjects shall be 50.
2.	**Aliskiren**	The Committee was informed that the Parliamentary Standing Committee (PSC) of the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on the functioning of CDSCO. The committee had made various recommendations and observations on approval of certain new drugs. Aliskiren is one of such drug. This Directorate had approved Aliskiren 150/ 300 mg tablets for treatment of essential hypertension in adults. As per action taken report, it was decided that the drug would be referred to NDAC for examination and review the issue related to continue marketing of these drugs and updating of the product monograph in light of recent knowledge and regulatory changes overseas. Accordingly, the firm presented detailed data including international regulatory status, Indian clinical data, recent safety updates following ALTITUDE and ASTRONAUT results. The drug is approved and marketed in 106 countries including key countries like US, EU, Switzerland and Japan. The drug was approved based on the global study CSPP100A2304 wherein a total of 49 subjects were enrolled form India. Firm stated that they have submitted PSUR covering the period from Oct, 2007 to Sep, 2012. Considering all the above aspects, the Committee felt that there is need of verification of safety data by Pharmacovigilance Programme of India.

3.	**Ambrisentan**	The Committee was informed that the Parliamentary Standing Committee (PSC) of the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on the functioning of CDSCO. The committee had made various recommendations and observations on approval of certain new drugs. Ambrisentan Hydrochloride is one of such drug. This Directorate had approved the Ambrisentan 5mg/10mg (Tablets) on 28th May. 2010, for the treatment of pulmonary arterial hypertension (WHO Group I) in patients with WHO class II or III symptoms to improve exercise capacity and delay clinical worsening. As per action taken report, it was decided that the drug would be referred to NDAC for examination and review the issue related to continue marketing of these drugs and updating of the product monograph in light of recent knowledge and regulatory changes overseas. Accordingly, the firm presented detailed efficacy and safety data including international regulatory status, global and Indian patient exposure, published clinical studies. Firm also presented adverse events reported from March 2012 to till date from India and data from study under ARIES programme. The Committee noted the following: • The drug ambrisentan is used for Pulmonary Arterial Hypertension (PAH) condition which is infrequent condition and there is no safer alternatives for the management; • In other countries the drug has been given orphan drug status; • It is much better therapeutic option as compare to the existing drugs such as bosentan because of its much better safety profile. The Committee opined that further safety data should be collected by closely monitoring. The firm should comply with PSUR submission as per existing Drugs and Cosmetics Rules i.e for a period of four years from the date of marketing.
4.	**Everolimus**	The Committee was informed that the Parliamentary Standing Committee (PSC) of the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on the functioning of CDSCO. The committee had made various recommendations and observations on approval of certain new drugs.

		Everolimus is one of such drug. This Directorate had approved the Everolimus 0.25, 0.5, 0.75 mg and 1 mg (Tablet) indicated as prophylaxis of organ rejection in adult patients as low to moderate immunological risk receiving allogenic renal transplants in combination with cyclosporine and corticosteroids As per action taken report, it was decided that the drug would be referred to NDAC for examination and review the issue related to continue marketing of the drug and updating of the product monograph in light of recent knowledge and regulatory changes overseas. Accordingly, the firm presented detailed data including international regulatory status, published clinical studies including data from ASCERTAIN Study and ELEVATE RAD 2429 wherein Indian subjects were included. The drug was approved The firm informed that the total new patients receiving everolimus from 2005 to 2013 are 3000, the number of patients on everolimus currently are approx 2000 + and the number of patients discontinued everolimus are approx 30%. The major reasons for discontinuation were financial reasons, side effects etc. It was further informed that total AEs / SAEs reported with everolimus till date (all grade) are 59 cases only. It was also stated that PSUR covering the period of 2003 till 2012 have already been submitted. Considering all the above aspects, the Committee felt that there is need of verification of safety data by Pharmacovigilance Programme of India.
5.	**Iodixanol Injection 270mgl/ml & 230mgl/ml**	The drug Iodixanol Inj. An iodinised contrast medium was approved in India long back only for administration in adults. The firm has proposed for use in children as an extension of the approved indication. The drug is approved in children in 70 countries including USA. The firm had conducted a global trial also in India on adults subject only. The committee has recommended for submission of phase –III clinical study in children for further review of NDAC .
6.	**Amlodipine + Indapamide**	The firm has contacted survey in 500 doctors across the country with quick responses on specimen questionnaires. The methodology of these questioning was validated prior to the actual data collection. 438 doctors had responded.

		The Committee opined that the higher strength of FDC is already approved. The proposed FDC of Indapamide 1.5 mg SR +Amlodipine 2.5 mg is recommended for manufacturing and marketing in elderly patients of age more than 65 years.
7.	**Indapamide+PeridoprilErbumin**	Firm presented BE study data before the committee. The proposed strength is approved in EU, France, Canada etc. Firm also presented published data on the FDC. The committee recommended for manufacturing and marketing the proposed strength of FDC with the condition that it shall be supplied in a monocarton with package insert mentioning warning of Hypokalemia. Further firm shall conduct a Phase IV trial on at least 500 patients on the proposed strength.
8.	**Atorvastatin ER +Choline Fenofibrate DR**	The committee recommended for a bridging safety & efficacy study of the FDC. Protocol may be accordingly submitted before the committee.
9.	**Metoprolol Succinate USP eq. to Metoprolol Tartrate IP+ TelmisartanIP+Amlodipine Besilate IP eq. to Amlodipine IP**	All three drugs are individually approved in India. However it is a new combination. Three drug combinations had a diuretic as one of the three drugs. It was opined by the committee that nowhere else is a three drug combination without a Diuretic approved at the present time. It was also felt that such a proposed combination would cater to a very small population and hence the FDC is non essential. The committee therefore did not recommend the study.,
10.	**Erythropoietin (CRL121211 Version No. 2 dated July 12,2013)**	The firm presented the protocol for conduct of the comparative PK/PD study with Erythropoietin vide Protocol vide CRL121211 Version No.2 dated July 12, 2013. The Single IV dose comparative, open label, a cross over, three period study has been proposed with 21 days wash out period. HSA will be from Baxter (India) ltd. The proposed study will be for export registration in foreign country. The NDAC recommends the trial proposal wih following suggestions; 1. Also to include female subjects. 2. The haemoglobin lower limit should be 12.5 g/dL
11	**Eryhtropoetin (CRL121212 Version No. 2 dated July 12,2013)**	This pertains to Sub-cutaneous administration of EPO-HAS combination on 48 male subjects only to copare with “EPREX” branded similar formulation of Johnson & Johnson Ltd. The reference formulation is free of HSA but has Tween-80. The NDAC recommends approval of the proposed comparative PK / PD study wih following suggestions;

		1. Also to include female subjects 2. The haemoglobin lower limit should be12.5 g/dL.
12	**Methyl prednisolone oral Tablets.**	This is a phase III study with Methyprednisolone (Tablet) proposed by George Clinical. This is an academic study to evaluate the long- term efficacy and safety of oral Methylprednisolone compared to matching placebo, on a back- ground RAS Inhibitor therapy, in preventing kidney events in patients with IgA nephropathy and feature suggesting a high risk of progression. The study drug is approved in India. The total numbers of countries participating are 6 which include China, Hong Kong, Canada, Singapore, Australia and India. The inclusion criteria include patients with GFR up to 20 ml/min (Stage IV CKD) which is not because of cresentric glomerulo nephritis. Steroid alone in stable stage-IV CKD is not appropriate as the risk is far more than the potential benefit. One of the exclusion criteria is minimal change disease with IgA deposition. Without electron microscopy this exclusion criteria is invalid to differentiate from IgA with minimal change pathology. There is no investigation mentioned in the protocol to diagnose the latent TB which is one of the exclusion criteria. This is an important issue in patients with IgA and CKD, more so in Indian context. For such type of study requiring creatinine and proteinuria estimation and for consistency of the results a central Laboratory is essential. In view of the above the study protocol is not acceptable in this present form.
13.	**Telmisartan + Amlodipine + HCTZ**	This is a phase III study with **strength 1: Optidoz** - Telmisartan (20mg) + Amlodipine (2.5mg) + HCTZ (6.25mg). **Strength 2 - telsartan trio** : Telmisartan (40mg), Amlodipine (5mg), Hydrochlorthiazide (12.5mg) . The firm presented the advantages of triple drugs combination as compared to mono-therapy in management of hypertension. However the NDAC opined that at present there is no scientific justification for use of three drugs combination pill as starting therapy in stage 1 hypertension . Therefore the NDAC does not recommend approval of the study.

13. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 26.03.2014:-

The NDAC (Cardiology and Renal) deliberated the proposals on 26.03.2014 and recommended the following:-

Agenda no.	Drug name	Recommendations
1.	**Mipomersen Sodium Injection 200mg/ml**	The firm presented clinical data including safety and efficacy of the drug along with international regulatory status of the drug. The firm also presented the status of ongoing phase III clinical trial in India as part of global clinical trial wherein 40 patients from Indian sites were proposed to be recruited. The firm requested for clinical trial waiver on Indian subjects. The Committee noted that at present only six patients have been enrolled in this study and the study is still ongoing. After deliberation, the Committee did not recommend for waiver of clinical trial in Indian subjects. The firm should submit clinical trial report etc. of the ongoing study after completion before the Committee for further review.
2.	**Azilsartan Medoxomil 40mg/80mg tablets**	The firm presented the proposed clinical trial protocol. The Committee examined the protocol and observed that the present study involved newly diagnosed hypertensive subjects and there is no need of wash out period. So admitting 20 patients in ICU setting does not apply to this study. Therefore, the Committee recommended that its earlier recommendation will remain same.
3.	**Azilsartan Medoxomil 40mg/80mg tablets**	The firm presented revised Clinical Trial protocol as per the recommendation of Apex Committee. It was informed that first 20 patients will be studied in ICU setting and their safety data will be analyzed by the DSMB. After deliberation, the Committee recommended for the proposed study as per the revised protocol. Further on the basis of DSMB data, the Ethics Committee may permit the continuation of the study.
4.	**Moxonidine**	The firm presented the global safety and efficacy data of the drug. The Committee noted that the ADRs reported are comparable to ADRs of the same class of the

		drugs. After deliberation, the Committee recommended for continued marketing of the drug.
5.	**Canrenone 50/100mg Capsule**	The Committee was informed that the Committee in its earlier meeting had noted that the proposed drug aldosterone antagonist is not approved internationally for management of essential hypertension. The Committee did not agree for the conduct of study in present form. Now the firm has represented their case for reconsideration. The firm presented the clinical trial entitled as "Efficacy and Tolerability of Canrenone in the treatment of stage I Hypertension." The firm also presented the safety data. The Committee noted that no national or international Scientific body has ever recommended this drug as first line single agent for the treatment of stage I essential Hypertension. After deliberation and with the present knowledge, the Committee recommended that the current proposal to conduct clinical trial with Canrenone cannot be considered.
6.	**Everolimus**	The Committee noted that out of 406 adverse events 209 events were causally suspected. The Indian safety data is comparable to that of internationally data. After deliberation, the Committee recommended for continued marketing of the drug. The Committee also suggested that as the number of patients who were taking the drug is few, the firm should collect safety data from such patients.
7.	**Treprostinil**	The committee reviewed the minutes of NDAC held on 27/09/13 and the presentation made by the applicant during this meeting. The committee recommends for the conduct of the study at the proposed centers/ trial sites.
8.	**Treprostinil**	The committee reviewed the minutes of NDAC held on 27/09/13 and the presentation made by the applicant during this meeting. The committee recommends for the conduct of the study at the proposed centers/ trial sites.
9.	**Miscellaneous Agenda Review and finalization of minutes of meeting held on 24.01.14 being quorum was not completed.**	Earlier recommendation made by NDAC Cardiology and Renal Committee held on 24.01.2014 in respect to various proposals were circulated as the quorum was not met during the last meeting, the Committee discussed the recommendations in details and agreed to the recommendation made by earlier members of the Committee for further action by the office of DCGI.

14. RECOMMENDATIONS OF THE NDAC (CARDIOLOGY AND RENAL) HELD ON 28.05.2014:-

The NDAC (Cardiology and Renal) deliberated the proposals on 28.05.2014 and recommended the following:-

Agenda no.	Drug	Recommendations
1.	**Azelnidipine Tab. (8mg / 16mg)**	The firm presented the revised Clinical trial protocol for conducting study with Azelnidipine 8mg / 16mg tablet vs Amlodipine 5mg/10mg. The committee noted that in most of the patients Amlodipine 5mg is the initial dose. Many patients respond adequately to this dose. After detailed deliberation therefore the committee agreed for the conduct of the study with Azelnidipine 8mg / 16mg tablet vs Amlodipine 5mg/10mg tablet as per the protocol submitted by the firm.
2.	**Dabigatran Etexilate Capsules**	The committee was appraised that the firm was granted permission for the import and marketing of Dabigatran Capsules subject to the condition that phase –IV clinical trial is required to be conducted in Indian patients. Accordingly the firm submitted CT protocol. The proposal was deliberated in NDAC meeting held on 27/9/13.The committee had recommended that the firm should submit initially the Indian subset analysis data of study No. 1160.71 study name “RELY-ABLE” before the committee. Now the firm presented India specific subset analysis report of the study No. 1160.71. The firm then requested for the waiver of requirement of conduct of Phase-IV study in Indian patients. The committee noted that the firm has generated clinical trial data on 126 patients under the said study for 4.5 years. The efficacy and side effects of the drug in these patients are in line with the global trials. Therefore, the committee recommends that the firm be granted exemption for the need of phase-IV clinical study.

3.	**Everolimus**	The Committee was apprised that earlier the proposal of the firm for conduct of **Phase - IV** clinical trial with **Everolimus** in Kidney transplant cases was deliberated in NDAC (Cardiology and Renal) meeting held on 27.09.2013. And the Committee recommended that firm should address the following ethical concerns for further review by the Committee: • Management of the graft deterioration during the study. • Continuation of the drug to the trial subjects after completion of the study as the drug is to be used for life long. Now, the firm presented reply in response to the above concerns made by the committee. However the reply was deemed inadequate. The company has agreed to provide Everolimus at 50% of the cost after the one-year study period. After deliberation the Committee recommends the proposal subject to the condition that the firm would provide free medical management of the patients having SAE including the graft failures during the study till the SAEs resolves, which may be lifelong.
4.	**Sevelamer Carbonate Dispersible Tablet (400/800mg)**	The data presented by the firm is inadequate and the committee opined that there is no need for such product as the same drug is already approved in tablets and powder formulation (in sachet). Hence the committee did not recommend for the proposed formulation.
5.	**Enalapril maleate mouth disintegrating strips 2.5/5/10 mg**	The firm presented before the NDAC committee. However the advantages claimed for the new proposed formulation are neither convincing, nor offering significant advantages over the currently available products. Therefore the NDAC panel of experts did not recommend the proposed formulation.
6.	**Olmesartan Medoxomil+Chlortlhalidone**	This proposal has been withdrawn by the applicant firm.
7.	**Atenolol + Amlodipine**	The applicant firm has applied for permission to manufacture and market FDC of Atenolol 25mg/50mg + Amlodipine Besylate eq. to Amlodipine 5mg/5mg hard

	Besylate	gelatin capsulesd market Fixed Dose Combination of Atenolol 25mg/50mg + Amlodipine Besylate eq. to Amlodipine 5mg/5mg hard gelatin capsules for the treatment of hypertension and chronic stable coronary insufficiency. The firm presented before the NDAC committee. However the advantages claimed for the new proposed formulation are neither convincing, nor offering significant advantages over the currently available products. Therefore the NDAC panel of experts did not recommend the proposed formulation.
8.	**Idaruzumab (B1655075)**	The firm has applied for the grant of permission to conduct a phase -III case series clinical study of the reversal of the anticoagulant effects of **Dabigatran by intravenous administration of 5.0 g (50 mg/ml) Idarucizumab (B1655075)** in patients treated with dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures. The Firm has presented its proposal before the NDAC experts and the committee after deliberation recommends approval of the trial as it is also an unmet need.
9.	**Mipomersen**	This Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Safety and Efficacy of Two Different Regimens of **Mipomersen (Sterile Solution, 70 and 200 mg)** in Patients with **Familial Hypercholesterolemia and Inadequately Controlled Low-Density Lipoprotein Cholesterol was approved** The firm has now presented protocol amendment-1. The committee reviewed and opined that there is an unmet need for this condition and recommends the approval of the said amendment 1.
10.	**Selexipag Film Coated Tablet 200mcg**	This Long-term, single-arm, open-label study, to assess the safety and tolerability of **Selexipag (ACT-293987)** in patients with pulmonary arterial hypertension (PAH) was permitted on 27 Dec 2011 to M/s. Pharma Leaf India Pvt Limited, Bangalore 560052. The protocol amendment version -6.0 dated 14/12/11 was approved after deliberation in the NDAC on 21/3/2013. The investigational drug **Selexipag** is not yet approved any wherein the world. The firm has presented data / reports before the panel

		of experts of NDAC and the committee recommends approval of the protocol amendment for rollover of the patients into the open label phase protocol with a condition that the interim analysis reports of the patients under treatment in other protocols shall be submitted for NDAC review within two months w.e.f. 01/June/14
11.	**UT-15C (Treprostinil diethanolamine)**	The open label, Phase-III, Extension trial with the drug was approved on 06/11/2008 for the treatment of pulmonary Artrial Hypertension (PAH). The CRO (applicant) firm has now submitted the trial protocol amendment -5. T The committee opined that there is a major protocol amendment .The outcome of the study TDE-DU-101 is to be presented to the committee along with the safety data for this SR formulations before considering this protocol amendment. The committee also opined that there is unmet medical need for PAH.
12.	**Erythropoietin Injection**	The firm has sought for permission of a new dosage claim in **Posology** section of Package insert i.e. during the maintenance phase EPREX can be administered either 3 times per week, and in the case of subcutaneous administration, once weekly or once every two weeks. Appropriate adjustment of dose and dose intervals should be made in order to maintain hemoglobin values at the desired level: Hb between 10 and 12g/dl (6.2-7.5mmol/l) extending dose intervals may require an increase in dose. The maximum dosage should not exceed 150IU/kg 3 times per week, 240IU/kg (upto maximum of 20,000IU) once weekly or 480IU/kg (upto a maximum of 40,000IU) once every 2 week. The NDAC after deliberation recommended approval of the proposed changes in the package insert.