New Drugs recommended by NDAC for marketing authorization in the country without local clinical trial (Till August 2012)						
Sr. No.	**Drug Name**	**Indication**	**Date of Approval**	**Opinions of Experts were sought on**	**Reasons presented by firms for waiver of local CT before the committee**	**NDAC Recommendations**
1	**Cabazitaxel**	In combination with prednisone for treatment of patients with hormone-refractory metastic prostrate cancer previously treated with a docetaxel-containing treatment regimen.	**16.11.11**	Safety, efficacy as well as essentiality and desirability in the country and requirement of conducting local clinical trial in Indain patients before the grant of marketing authorization of the drug	The proposal was examined by the committee through circulation and the firm presented the following reasons in support of CT waiver:	The proposal was examined through circulation by NDAC-Oncology & Hematology and CT exemption and approval was granted based on written opinion from 9 experts of the committee.
2	**Abiraterone Acetate**	In combination with prednisone for the treatment of patients with metastatic castration-resistant prostrate cancer who have received prior chemotherapy containing docetaxel.	**16.12.11**	Safety, efficacy, essentiality and desirability of the drug and whether based on the data submitted, permission to import and market the drug can be granted to the firm, without conduct of local clinical trial as per the provision of Drugs and Cosmetics Rules.	Firm presented the following points to the committee: -Prostate cancer is an important cause of cancer mortality in the aging population -Androgen stimulation from the tumor & adrenals remain important reasons for tumor growth despite hormonal treatment -Significant unmet need in the management of CRPC patients post-Docetaxel- No Standard of Care -Abiraterone Acetate, an orally active androgen biosynthesis inhibitor with unique MOA inhibits androgen production from all sources including Testes, Adrenal & Tumor tissues -Abiraterone provides significant survival advantage irrespective of Age, PSA status, radiographic progression, prior chemotherapies -Drug Is well tolerated with negligible myelosuppression, which is critical for Docetaxel treated patients.	Approved with condition of conducting Post Marketing trial (Phase IV) in Indian population to monitor the adverse effects. Report of post marketing trials ongoing in other countries when completed should be submitted.For change in prescribing information/package insert based on clinical trial being conducted as per condition of US FDA approval should be communicated to the office of DCG(I).
3	**Crizotinib**	For the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK) – positive as detected by an FDA-approved test.	**16.12.11**	Opinion about the requirement of clinical trial on Indian population if any and whether based on data/information submitted permission may granted to the applicant to import and market Crizotinib Capsule in the country	Requested for approval of the drug based on the global clinical trial data, unmet medical need of the product and also highlighted the expedited approval of the drug given by US-FDA due to the above mentioned reasons like efficacy, safety and unmet medical need etc.	Approved with the condition that structured post marketing trial (Phase 4) should be conducted in Indian population. Report of post marketing trials ongoing in other countries when completed should be submitted.

4	**Degarelix**	For the treatment of adult patients with advanced hormone dependent prostrate cancer.	**19.01.12**	Safety, efficacy as well as essentiality and desirability of the Degarelix injection in the country and requirement of conducting local clinical trial in Indian patients before the grant of marketing authorization of the drug	During presentation to the NDAC firm stated the following reasons for early approval of the drug: - Degarelix if approved will fill an important gap in today's treatment protocol in India. - It is the latest and safest GnRH receptor blocker in a novel drug delivery system - Rapid & Sustained onset of action compared to GnRH agonists. - Safety and efficacy of the drug as observed during international studies (Phase I, II, III)	Approved with the condition that data on survival rate of patients with advanced prostate cancer treated with Degarelix should be submitted to the office of DCG (I) before formal approval is granted. Also Post Marketing (Phase IV) trial should be conducted. Report of trials ongoing in other countries when completed should be submitted.
5	**Eribulin Mesylate**	For the treatment of patients with locally advanced or metastatic breast cancer who have progressed after at least two chemotherapeutic regimens for advanced disease. Prior therapy should have included an anthracycline and a taxane unless patients were not suitable for these treatments.	**27.01.12**	Safety, efficacy, essentiality and desirability of the drug Eribulin Mesylate solution for injection 0.44mg/ml in the country and also requirement of conducting local clinical trial before the grant of marketing authorization of the drug.	Firm presented the following points to the committee:1. The patient population with locally advance or refractory MBC have limited treatment options & is an area of unmet medical need with no single agent demonstrating increase in Overall survival 2. Eriblin fulfils the unmet medical need being the only single agent chemotheraputic agent demonstrating an increase in overall survival (OS) in heavily pre-treated MBC (Median 4 prior chemotheraputic agents) & the same is achieved with a manageable safety profile 3. Eribulin has shown a lower incidence of severe neuropathy (grade 3/4) as compared to ixabepilone & pacletaxel 4. Incidence of grade 3/4 neutropenia is comparatively less with Eribulin than with ixabepilone, vinorelbine & docletaxel as observed from Phase III trials cumulative data 5. Eribulin exhibited favorable safety profiles in Study 221 and Study 305 & has been evaluated in >1200 patients in Phase II & Phase III trials. 6. Eribulin showed no ethnic differences in the pharmacokinetic data between Japanese and US populations. 7. Eribulin also has a relative ease of administration, short infusion time (2-5 mins) & so far has shown no requirement for premedication to prevent hypersensitivity reactions & a favorable drug interaction profile. 8. Proposed precautions and dose adjustments will allow the toxicity of eribulin to be managed appropriately 9. Eribulin is listed as a preferred single choice agent in treatment of MBC in NCCN guidelines & also listed as new cytotoxic agent for MBC in ESMO guidelines 10.Chemotherapy practices for breast cancer management is near similar between India and other countries, and in absence of pharmacokinetic differences due to sex, race or age with Eribulin, we believe that safety & efficacy data obtained in the US/EU and Japan could be extrapolated to Indian patients.	Recommended for approval subject to condition that Phase IV clinical trial on 200 patients should be conducted. Protocol etc. for the Phase IV clinical trial should be submitted to the office of DCG(I) within 1 month of approval and enrolment of patients should be initiated within 3 months of approval. The study should be completed within 2 years of launching the product in the market.
6	**Plerixafor**	In combination with Granulocyte Colony Stimulating Factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma.	**31.01.12**	Safety, efficacy, essentiality and the desirability of Plerixafor solution for sub-cutaneous injection 20mg/ml in the country and requirement of conducting local clinical trial in Indian Patients before the grant of marketing authorization of the drug	Firm requested for approval of drug without local CT and presented data from international CT of the drug and also highlighted the following key points: - Unmet medical need - Plerixafor is well tolerated - Provides a means of getting failed mobilizers to HSCT which is current SOC - Allows a greater number of patients the opportunity to proceed to a therapeutic stem cell transplant	Recommended for approval subject to condition that Phase IV clinical trial on 50 patients (as it is a rare disease) should be conducted. Protocol etc. for the Phase IV clinical trial should be submitted to the office of DCG(I) within 1 month of approval and enrolment of patients should be initiated within 3 months of approval. The study should be completed as early as possible. During the Phase IV trial, subjects should be given free medication.

7	**Mucotrol™ concentrated oral gel wafer**	For the management of pain and relief of pain, by adhering to the mucosal surface of the mouth, soothing oral lesions of various etiologies, including oral mucositis/stomatitis (may be caused by chemotherapy or radiotherapy). Irritation due to oral surgery and traumatic ulcers caused by braces or ill fitting dentures of diseases and for diffuse apthous ulcers.	**07.03.12**	Safety, efficacy, essentiality and desirability of theMucotrol Concentrated Oral Gel Wafer in the country and requirement of conducting local clinical trialin Indian patients before the grant of marketing authorization of the drug.	Firm presented following points to NDAC for waiver of CT: -The Mucotrol TM has been approved by US FDA under section 510(k) Premarket notification-so no clinical data has been submitted to US FDA for the approval of this product. The ingredients of the Mucotrol TM are either excipient or ingredient used in Traditional Medicine of India. Mucotrol TM work mechanically and locally, no systemic action. Mucotrol is a poly ingredient formulation with no standard formulation to determine bioequivalence.Moreover, Literature reveals that currently available treatment for chemotherapy induced or radiation therapy-induced mucositis are of limited efficacy. The available local treatment was short lasting as the drug remains in contact with the mucosa for a short time and same drugs has poor palatability, compromising the therapeutic benefits. No known interactions with other medications.Mucotrol TM as an oral wafer formulation has good taste and it is in contact with the wound for a longer time. Additionally it is -Sugar free and non irritating.Published Clinical trial of Mucotrol TM in Indian population-safety and Efficacy data established in Indian population, sponsored by M/S Belcher Pharmaceuticals Inc. at Nizam Institute, Hyderabad.	Recommended for approval subject to As regards to the waiver of clinical trial requested by the firm, committee recommended for waiver of clinical trial in public interest in view of limited therapeutic medication. Recommended for marketing approval subject to condition that an open label Phase IV clinical trial on 400 patients should be conducted. Protocol etc. for the Phase IV clinical trial should be submitted to the office of DCG(I) within 1 month of approval and enrolment of patients should be initiated within 3 months of approval. The study should be completed within 6 months of launching the product in the market.
8	**FDC of Nutrineal PD4 with 1.1% Amino acid Solution (Sterile solution for intraperitoneal dialysis)**	Nutrineal Supplements for malnourished renal failure patients (Albumin concentration lower than 35g/litre) being maintained on peritoneal dialysis.	**18.04.2012**	Safety, efficacy and essentiality of FDC of Nutrineal PD4 with 1.1% Amino acid Solution for peritoneal dialysis for the said indication in the country and requirement of clinical trial in Indian patients before the grant of marketing authorization of the drug	Firm requested for waiver of clinical trial and submitted following reasons to the committee based on international data: • An unmet need as nutritional supplement for malnourished renal failure patients • Nutrineal is available across the globe for 18 years and currently in around 50 countries • Enough clinical experience in clinical studies as well as real world clinical practice	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 an 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 Jonstone 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.

9	**Etravirine**	In combination with other antiretroviral agents for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to an NNRTI and other antiretroviral agents. It should be used only in situations where other treatments have failed or cannot be used because of side effects.	**26.04.12**	Essentiality & desirability of the drug and whether based on data submitted permission to manufacture & market etravirine in the country may be granted to the applicant and opinion on the requirement of local clinical trial if any, in Indian population before its approval in the country	Firm presented following points to NDAC for waiver local CT and approval of drug: -A significant proportion of HIV infected patients experience treatment failure despite the effectiveness of multiple drug combination therapy. The proportion of new HIV infections that involve drug-resistance virus is increasing. Most of the patients (89%) have one or more mutations associated with NNRTI resistance. Etravirine is designed to work against HIV that is resistant to the currently available NNRTIs and shows greater effectiveness against regimen without etravirine. -After 10 years of having just one NNRTI-based regimen available, etravirine provides an important new sequential NNRTI option. Combined with other agents with activity against highly drug-resistant virus, we can now obtain complete HIV suppression in the vast majority of experienced patients. -Etravirine fills an important gap in the NNRTI class, being able to achieve viral suppression in the majority of patients with resistance to other NNRTIs, with favorable tolerability, few interactions with other ARVs, and an acceptable dosing schedule and pill burden.	Committee recommended for giving permission to market the drug subject to the following conditions:-i) It should be used only in situations where other treatments have failed or cannot be used because of side effects. For such situations, there is an unmet need of anti HIV drugs and local clinical trial is waived off. ii) The formulation should be tested at IPC before launching the product in the market. The other applicants for manufacturing permission should conduct single dose Bioequivalence study in Indian subjects and the data should be submitted to DCG(I) for his consideration and approval.
10	**Lipiodol UF**	In Diagnostic Radiology:Lymphography and Diagnosis of liver lesions. (Diagnosis of the spread of malignant lesions, whether hepatic or not, by selective hepatic arterial injection). In Interventional Radiology:Embolization with surgical glues. (In association with surgical glues during vascular embolizations). In Endocrinology: Prevention of iodine deficiency disorders. (This treatment should only be used when other methods of supplementation, particularly iodization of salt and/or drinking water, cannot be undertaken).	**6.08.2012**	Whether based on data/information submitted permission may granted to the applicant to import and market Lipidol ultra fluid in the country and opinion about the requirement of clinical trial on Indian population, if any.	Firm presented the following reasons to the committee: • “Lipiodol” is an iodinated contrast agent for radiology developed in 1901. • This product has been marketed worldwide since 1948 and is currently registered in about 50 countries including European countries, USA and Japan. • It is also registered on WHO list of Essential Drugs since 1990 for its therapeutic applications for Iodine deficiency disorders. • Over 3000 clinical trial and subsequent publication have also been done on “Lipiodol”. Therefore, the safety and efficacy profile of the product is well established worldwide. This product is only iodinated oil for the Indian market. It is a life saving drug.	The committee opined that there is an unmet medical need for the product for diagnosis of various disease conditions and the drug is already being used in the country through personal permit also. Therefore there is no need for local clinical trials. The committee recommended for giving permission to market the product subject to condition that Phase IV clinical trial should be conducted on atleast 100 Indian subjects. The protocol for the Phase IV study should be submitted to the office of DCG(I) within 1 month of permission and the study should be initiated within the period of 3 months.

11	**Nelarabine**	For the treatment of patients with T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) whose disease has not responded to or has relapsed following treatment with at least 2 chemotherapy regimens.	**Yet to be approved**	Safety, efficacy as well as essentiality and desirability of the Nelarabine injection 5mg/ml in the country and requirement of conducting local clinical trial in Indian Patients before the grant of marketing authorization of the drug.	Firm requested for waiver of clinical trial and submitted following reasons to the committee based on international data: -Clinically meaningful benefit as single agent in T-cell ALL/LBL -Pharmacological selectivity for T-cells *Consistent demonstration of CR >Second and third line patients >Refractory patients >Children and adults *CR durable and allowed time for transplantation *Demonstrable survival at one year T-ALL/T-LBL ≥ 2nd relapse or refractory disease -Poor prognosis and no standard of care -Acceptable safety profile of Nelarabine -Expected & manageable non-neurological (incl. hematologic) adverse events for indicated population Meets a significant unmet medical need -No proven effective alternative therapy available for T-ALL and T-LBL -Overall favorable benefit - risk profile for the proposed population of relapsed or refractory patients.	Experts opined that currently there is no recommended 3rd line therapy for the treatment of patients with T-cell lymphoblastic lymphoma. Therefore there is an unmet need for this drug for this subset of patients. Local clinical trial can be waived off. However the firm should submit detailed comparative evaluation of Chemical and Pharmaceutical data of Nelarabine bulk and formulation of the firm vis-à-vis that of Innovator's. The firm should also conduct single dose bioequivalence study in patients with T-cell lymphoblastic lymphoma with their formulation in comparison to that of Innovator's after getting protocol etc approved from the office of DCG(I). If above data is found satisfactory the product can be approved for marketing subject to Phase IV clinical trial.
12	**Fingolimod**	For the treatment of adult patients with relapsing-remitting multiple sclerosis with high disease activity.	**Yet to be approved**	Safety, efficacy as well as essentiality and desirability of the drug Fingolimod Hydrochloride 0.5mg Capsule and requirement of conducting local clinical trial in Indian patients before the grant of marketing authorization of the drug in the country.	Firm presented the non-clinical and clinical data of fingolimod from international studies to the committee alongwith the following key points: - Fingolimod has demonstrated convincing efficacy, both with respect to placebo and a current first-line therapy in patients with relapsing MS. -At the proposed dose of 0.5 mg, fingolimod has demonstrated an acceptable safety profile which can be further enhanced by the risk management plan. - Given the robust efficacy plus the convenience of once-daily oral administration, fingolimod offers significant benefits over current first-line therapies, including direct demonstration of superiority to IFN β-1a - In considering the totality of fingolimod data and in the context of the current MS therapeutic landscape, the benefit-risk assessment of once daily oral fingolimod 0.5 mg is considered to be favourable	Recommended for approval for manufacture and marketing the drug in the country subject to condition that the singe dose BE study is carried out and product is proven to be bio equivalent with the innovator product and after approval of the drug, the Phase IV clinical trial should be conducted on 100 subjects within a period of 2 years. The protocol for the phase IV study should be submitted within 1 month of approval of the drug to DCGI for approval. The Recruitment shall be initiated within one month of approval of protocol and status should be submitted to the office of DCGI on monthly basis. Recruitment of subjects should be at least at the rate of 25% of the total subjects quarterly. The interim analysis of the data shall be carried out every six month after 1st recruitment of the patient and submitted to the office of DCG (I).

13	**Tolvaptan**	For the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium < 125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure, cirrhosis, and Syndrome of Inappropriate Antidiuretic Hormone (SIADH).	**Yet to be approved**	Safety, efficacy as well as essentiality and desirability of the drug Tolvaptan 15mg/30mg tablet and requirement of conducting local clinical trial in Indian patients before the grant of marketing authorization of the drug in the country.	Firm presented the following points in support of their claim for waiver of clinical trial: Acute heart failure syndromes (AHFS), defined as rapid development of signs and symptoms of heart failure (HF) are a major public health problem Although existing therapies for AHFS, such as vasodilators and diuretics, effectively relieve signs and symptoms during the hospitalization,the dilemmas are high mortality (10%) and re-hospitalization (30%) rates in the first 60–90 days post-discharge, worsening renal function and hyponatremia. In these patients, congestion or fluid overload due to elevated left ventricular (LV) filling pressures manifests as dyspnoea, jugular venous distension (JVD), and/or oedema and increase in body weight.Blocking AVP leads to effective aquaresis, improvements in hemodynamics and renal function parameters weight loss, and normalization of serum sodium, without changes in blood pressure or heart rate.Overcomes the key issue of increased vasopressin levels. Allows solute free aquaresis .Greateraquaresis than furosemide or HCTZ without hyponatremia or hypokalemia .Can be useful to neurosurgeons where 30% patients have SIADH sec to subarachnoid hemorrhage . Since rapid correction of hyponatremia (>12 mEq/L/day) may cause osmotic demyelination caution should be advised with concomitant use of tolvaptan and hypertonic saline.	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).
14	**Rilpivirine**	For the treatment of human immunodeficiency virus type 1 (HIV 1) infection in antiretroviral treatment naïve adult patients (patients who have never taken HIV therapies, and are starting HIV therapy for the first time).	**Yet to be approved**	Safety, efficacy, essentiality and the desirability of Rilpivirine 25mg tablet in the country and requirement of conducting local clinical trial in Indian patients before the grant of permission to manufacture and market of the drug.	Firm presented the following salient features of Rilpivirine to the committee alongwith other clinical and non-clinical data: -Active against NNRTI-resistant strains of HIV -Convenient once daily dosage regime -Efficacy non-inferior to efavirenz -Can be combined with tenofovir and emtricitabine -Less risk of neurological and psychiatric adverse events compared to efavirenz -Less disturbance in serum lipid levels compared to efavirenz -No teratogenicity in animal studies unlike efavirenz -Does not interact with hormonal contraceptives -Fewer discontinuations due to adverse events -May spare use of protease inhibitors in those intolerant to EFV/NVP -Construct a OD regimen in women of child bearing potential in resource limited settings with limited access to RTV boosted PIs.	The drug is indicated for HIV which is a serious and life threatening disease. Committee recommended for approval of the drug subject to post marketing trial (phase IV trial). However before approval the firm should conduct single dose bioequivalence study and the data should be submitted to the office of DCG(I).

15	**Vemurafenib**	Indicated in monotherapy for the treatment of adult patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.	**Yet to be approved**	Whether based on data/information submitted permission may granted to the applicant to import and market Vemurafenib tablet in the country and pinion about the requirement of clinical trial on Indian population, if any	Firm presented the following reasons to the committee in support of their request for CT waiver: Drugs and Cosmetics rule 1945: Schedule Y - Point no. 1.(3)- For drugs indicated in life threatening/serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the licensing authority Unresectable or Metastatic melanoma • Life Threatening\serious - > 50% mortality in India • Indian Health Scenario – Less incidence – accounts for 75% mortality of skin cancer related deaths • Vemurafenib – First in class, orally bioavailable ,selective inhibitor of BRAF V600 mutant kinase – Median overall survival of 15.9 months – Relative reduction of 63% in the risk of death – Relative reduction of 74% in the risk of disease progression – Favorable risk benefit profile.	The drug is indicated for treatment of unresectable or metastatic melanoma patients with BRAF V600 mutation which is a very rare disease in India. There is an unmet medical need of the medicine for such conditions.Therefore, the committee recommended for grant of permission to market the drug subject to condition that the firm should generate data on at least 12 Indian patients under the global clinical trial which is already been permitted to be conducted in the country. The drug should be got tested from IPC, Ghazibad before launching the product in the country.
16	**Panitumumab**	Indicated as monotherapy for the treatment of patients with EGFR expressing metastatic colorectal carcinoma with nonmutated (wild -type) KRAS after failure of jluoropyrimidine-, oxaliplatin-, and irinotecancontaining chemotherapy regimens.	**Yet to be approved**	Opinion whether the firm can be granted Market Authorization to import an market Panitumumab based on the Global clinical trial data submitted by the firm.	The firm has submitted data of global clinical Phase III studies study# 20020408 and #20030194 on 463 and 232 respectively ,patients describing the usefulness of this molecule in metastatic colorectal carcinoma.	NDAC experts recommended observed that there is an unmet need of this drug as it is indicated for life threatening disease, the treatment of patients with EGFR expressing metastatic colorectal carcinoma with non-mutated (wild -type) KRAS after failure of prior therapies. Therefore, the committee considered the waiver of local clinical trial and recommended for giving permission for import and market of the drug subject to condition that Phase IV study with the drug should be conducted in 50 Indian patients.The protocol for the Phase IV study should be submitted to the office of DCG(I) within 1 month of permission and the study should be initiated within the period of 3 months.