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Research Article

CONTEMPLATION ON APPROVED DRUGS IN INDIA FROM 1999 THROUGH 2011

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ABSTRACT

Objective: There is a change in the regulatory environment after a system of product patents in India since 2005. The objective of this study was to analyse the trends of drug approval in India during the period of 1999 to 2011.
Materials and Methods: The information about drug approvals was primarily obtained from the Indian regulatory agency website. For the drug products identified, the drugs were classified into fourteen main Anatomical Therapeutic Chemical (ATC) groups, single or combination products, types of dosage form, approvals for additional strength, approvals for additional indication and approvals for new dosage form.
Results: We identified 1506 approvals by the DCGI from 1999 to 2011, with a mean of 115.84±83.24 (SD) approvals per year (Median approvals per year: 79; Range: 23-264). The ATC groups containing over 10% of total approvals were N (nervous system), with 232 (15.4%); J (antiinfective for systemic use), with 204 (13.54%); A (alimentary tract and metabolism), with 192 (12.74%) and C (cardiovascular system), with 186 (12.35%). Since 2004, there is a rising trend for approval of products having drugs in combination. Total 448 new drugs were approved during the period of 1999 to 2011, with a mean of 34.46±8.14 (SD) new drug approvals per year (Median new drug approvals per year: 36; Range: 22-53).
Conclusions: These results show that there is a rising trend of approval for fixed dose combinations. The pattern of 'new drug' approval was flattened around the years when patent policy change was introduced.

Key words: Drug approval, ATC group, new drug, regulatory, fixed dose combination

INTRODUCTION

The approval of a drug product by the regulatory authorities is a lengthy process. Research and development of new drugs is an ongoing process and it often takes more than a decade to launch a new drug in the market[1]. The control of government regulatory agencies over the introduction of new drug products is an absolute necessity to assure the effectiveness and safety of new drugs.

The main regulatory body for the Indian pharmaceutical industry is the Central Drugs Standard Control Organization (CDSCO), which falls under the Ministry of Health and Family Welfare. The Drug Controller General of India (DCGI) is the controlling body for the CDSCO. The office of the Drug Controller General of India is responsible for the approval of new drug products and clinical trials. The DCGI office also monitors state drug-authorities, which are mainly responsible for granting drug manufacturing and retailing licenses.

Over the last 40 years, India's pharmaceutical industry has evolved from almost non-existent before 1970 to a world leader in the production of high quality drugs[2]. India has garnered a worldwide reputation for producing high quality, low cost generic drugs. The Indian pharmaceutical industry is a success-story ensuring that essential drugs are available at affordable prices to the vast population. The availability of drugs in the country has improved tremendously. From the level of being a major importer at the time of Independence, the country has become supplier to the World.

When only process patents were granted, the Indian drug houses had an advantage to lead the role as a world leader in the production of affordable generics. As per World Trade Organisation (WTO), from the year 2005, India granted product patent recognition to all new chemical entities (NCEs)[2]. It effectively ended over 35 years of protection for Indian companies and terminated legal reverse engineering or copying of patented foreign pharmaceuticals drugs. Since 2005, many multinational corporations (MNCs) began re-entering the Indian pharmaceutical market by setting up their own manufacturing, research and development (R&D) facilities.

As there is a tremendous change in the regulatory environment after a system of product patents in India, we considered it worthwhile to analyse the drug approval trends in India during the period 1999 to 2011.

MATERIALS AND METHODS

This report is based on the information available on the CDSCO website. The list of approved drug products was available from 1999 through 31st December 2011 at the time of analysis of these data. The information about the name of approved drug product, the indication/s and the date of issue of marketing approval was retrieved from the CDSCO website[3].

This information from the CDSCO website was entered and analysed using a Microsoft Excel worksheet (Microsoft Office 2010). For the drug products identified the following features were recorded: the ATC code as per WHO Anatomical Therapeutic Chemical (ATC) classification[4], single or combination product, dosage form, additional strength, additional indication/s and new dosage form/s. As per ATC classification system, the drugs were classified into fourteen main groups.

The complete information was not available for the biological products on the CDSCO website. Therefore it was decided to exclude biological products from the current analysis. We also excluded 20 veterinary drug products from the current analysis, which were approved by the DCGI during 1999-2011.

The approvals included drug products for additional indications, additional dosage forms, additional higher or lower strengths, new salts and combinations of previously approved drugs besides the products having a new molecule as a 'drug' ('new drug'). This aspect is considered while analysing the approved drug products and attention is paid to the analysis of approved 'new drug'.

RESULTS

The study identified total 1506 approvals by the DCGI from 1999 to 2011, with a mean of 115.84±83.24 (SD) approvals per year (Median approvals per year: 79; Range: 23-264). The year-wise distribution of total number of approvals is shown the table 1. Out of these 1506 approvals, 95 (6.3%) drug products were approved for additional indications, 34 (2.25%) drug products were approved for additional dosage forms, 165 (10.95%) drug products were approved for additional lower or higher strengths, four (0.26%) drug products were approved for additional pack size and 568 (37.71%) drugs were approved as fixed dose combination. The mean, median and range of drug product approvals are shown in table 2.

Table 1: Total Number of drug approvals in India, 1999-2011 (*n*=1506)

Year	Number of Approvals (in %)
1999	23 (1.52)
2000	28 (1.85)
2001	41 (2.72)
2002	56 (3.71)
2003	39 (2.58)
2004	76 (5.04)
2005	122 (8.1)
2006	161 (10.69)
2007	188 (12.48)
2008	264 (17.52)
2009	208 (13.81)
2010	221 (14.67)
2011	79 (5.24)
Total	1506

Table 2: Drug products approved per year in terms of mean, median and range; in various categories analysed

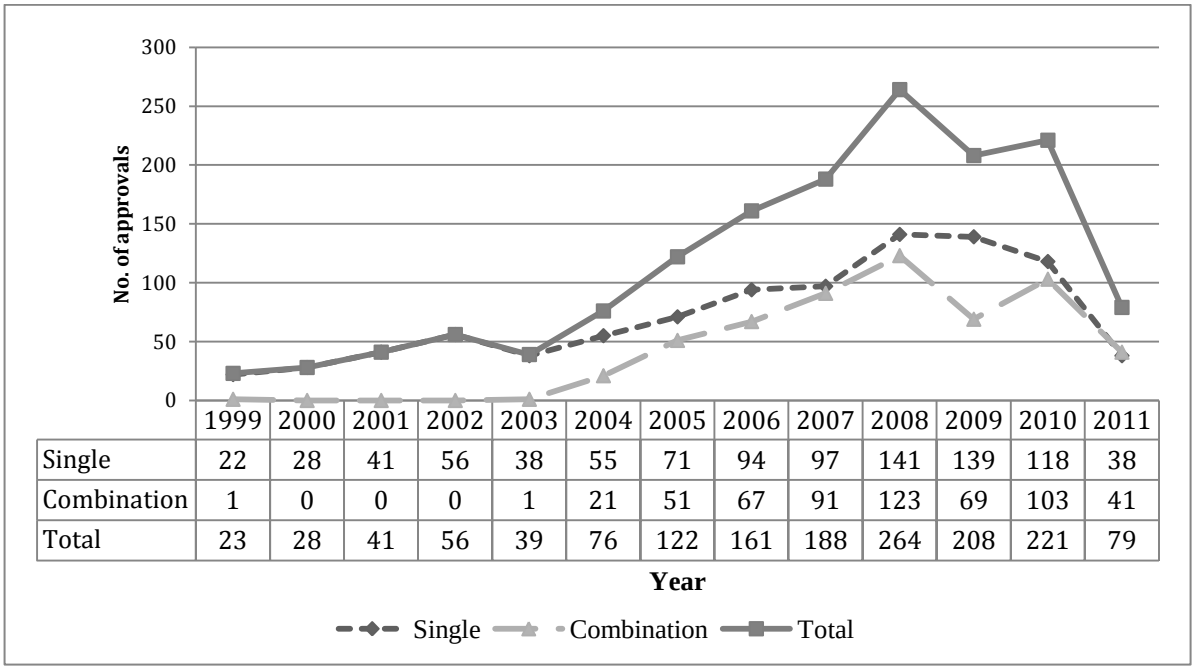
	Mean±SD	Median	Range
Total number of approvals (*n*=1506)	115.84±83.24	79	23-264
Single drug product approvals (*n*=938)	72.15±41.56	56	22-141
Combination drug product approvals (*n*=568)	43.69±43.94	41	0-123
'New drug' approvals (*n*=448)	34.46±8.14	36	22-53

When these 1506 approvals are analysed in terms of dosage forms, it is observed that 1026 (67.94%) approvals were for oral dosage forms, 197 (13.04%) were for parenteral dosage forms, 28 (1.85%) were for inhalation dosage forms, 226 (14.96%) were for topical dosage forms, 12 (0.79%) were for transdermal dosage forms and 21 (1.39%) were for other types of dosage forms. Other types of dosage forms included nasal spray for systemic use, lozenges, intranasal solution, plaster, implant, sublingual tablets, dialysis solution and contraceptive rings.

Table 3: The approved drugs (*n*=1506) in India categorised in Anatomical Therapeutic Chemical (ATC) groups

ATC Group	Number of Approvals (in %)
A - Alimentary tract and metabolism	192 (12.74)
B - Blood and blood forming organs	39 (2.58)
C - Cardiovascular system	186 (12.35)
D - Dermatologicals	108 (7.17)
G - Genito urinary system and sex hormones	56 (3.71)
H - Systemic hormonal preparations (excluding sex hormones and insulins)	10 (0.66)
J - Antiinfectives for systemic use	204 (13.54)
L - Antineoplastic and immunomodulating agents	102 (6.77)
M - Musculo-skeletal system	145 (9.62)
N - Nervous system	232 (15.4)
P - Antiparasitic products, insecticides and repellents	20 (1.32)
R - Respiratory system	115 (7.63)
S - Sensory organs	74 (4.91)
V – Various	23 (1.52)

The approvals are categorized in terms of ATC groups. The analysis is shown in the table 3. Classification of the approved drug products from point of view of therapeutic utility showed some interesting aspects. The ATC groups containing over 10% of total approvals were N (nervous system), with 232 (15.4%); J (antiinfective for systemic use), with 204 (13.54%); A (alimentary tract and metabolism), with 192 (12.74%) and C (cardiovascular system), with 186 (12.35%).



	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Single	22	28	41	56	38	55	71	94	97	141	139	118	38
Combination	1	0	0	0	1	21	51	67	91	123	69	103	41
Total	23	28	41	56	39	76	122	161	188	264	208	221	79

Figure 1: Time trends of drug approvals in India during 1999-2011 (*n*=1506)

The time-trend curve for all the approved drug products during the period from 1999 to 2011 is presented in figure 1. It also shows the drug products containing both, single or combination of drugs, which are plotted separately. The plot shows an overall rising trend, with the highest approvals in 2008 (*n*=264); in subsequent years the number of approvals are less. Since 2004 a rising trend is seen for approval of products having drugs in combination. This trend also peaks up during 2008 (*n*=123). Then it recedes in the subsequent years; with lowest number being in 2011 (*n*=41). The gap is being narrowed down between the approvals of single drug product and combination drug product in 2010 and 2011. Actually there are more number of approvals for combination products in 2011 (*n*=41) as compared to the approvals of single drug products (*n*=38). In other words, half of the approvals in year 2010 and 2011 are in the form combinations of the drugs.

Data is further analysed in terms of approved drug products containing single or combination of drugs, for different therapeutic categories. Figure 2 shows the drug products approved for each group of ATC classification. There are more number of combination drug products approved in Cardiovascular system (C) ATC group (*n*=106 for combination and *n*=80 for single). For Dermatologicals (D) ATC group and Antiparasitic, insecticides and repellents (P) ATC group also the combination drug product approvals are more in number as compared to the single drug product approvals. For Antineoplastic and immunomodulating agents (L) ATC group, there are more number of single drug product approvals as compared to the combination drug products (*n*=100 for single and *n*=2 for combination).

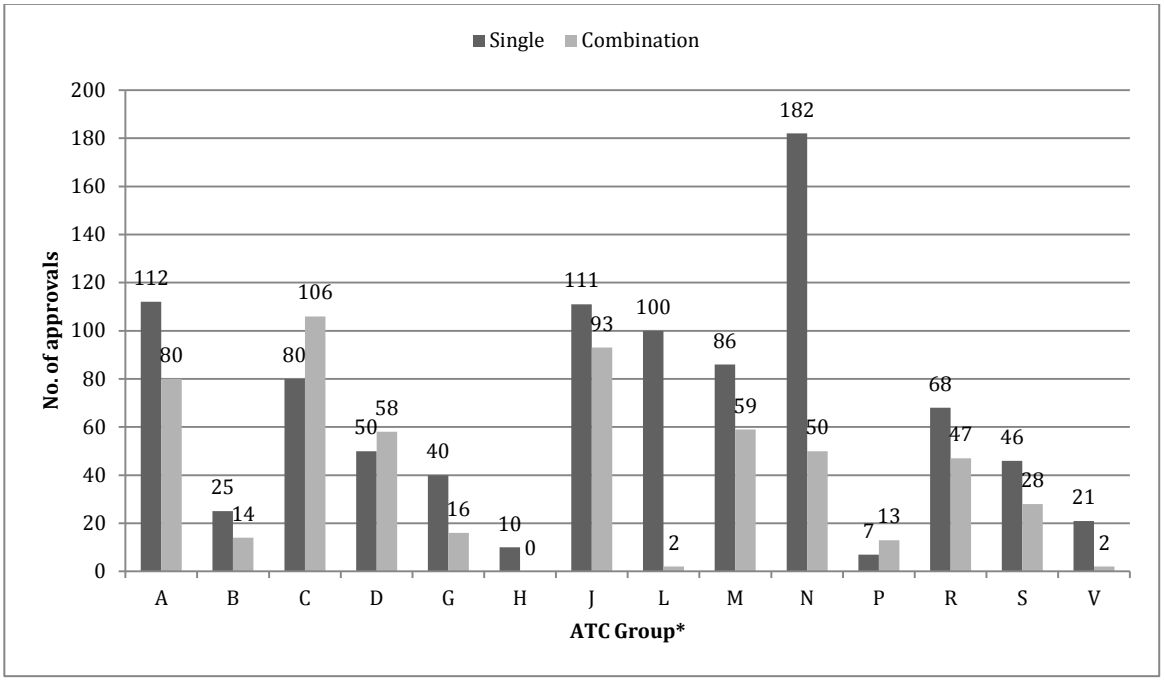


Figure 2: Drug approvals as single and combination products for fourteen ATC groups (*n*=1506)

***ATC Group: A (Alimentary tract and metabolism), B (Blood and blood forming organs), C (Cardiovascular system), D (Dermatologicals), G (Genito urinary system and sex hormones), H (Systemic hormonal preparations, excluding sex hormones and insulins), J (Antiinfectives for systemic use), L (Antineoplastic and immunomodulating agents), M (Musculo-skeletal system), N (Nervous system), P (Antiparasitic products, insecticides and repellents), R (Respiratory system), S (Sensory organs), V (Various).**

The approved drug products in all fourteen ATC groups were analysed from the point of view of year wise trends. There are more number of approvals for Nervous system (N) ATC group as compared to other groups in last 3 years (2009-2011); Antiinfectives for systemic use (J) ATC group had highest number of approvals in year 2006 and 2008. Similar higher numbers of approvals are exhibited in categories of Cardiovascular (C) and Musculo-skeletal system (M) during period 2005 to 2010 and 2006 to 2010 respectively. In case of about half of the categories (namely, A, C, D, J, M, N, R and S), there are more number of approvals from year 2005 to 2010. Categories B, G, H, L, P and V do not exhibit a trend of this kind.

The data is also screened from point of view of approved products having 'new drug'. The study identified total of 448 'new drug' approvals during 1999-2011; the year wise distribution being as follows: 22 (4.91 %) in 1999; 28 (6.25%) in 2000; 39 (8.7%) in 2001; 53 (11.83%) in 2002; 37 (8.25%) in 2003; 33 (7.36%) in 2004; 36 (8.03%) in 2005; 37 (8.25%) in 2006; 31 (6.91%) in 2007; 38 (8.48%) in 2008; 32 (7.14%) in 2009; 40 (8.92%) in 2010 and 22 (4.91%) in 2011. The DCGI has approved an average 34.46 'new drugs' per year during the period of 1999 to 2011 (Median 'new drug' approvals per year: 36; Range: 22-53). It is also noted that the number of 'new drug' approvals shows a rising trend from 1999 to 2002. However, after 2002 the pattern is almost flat; ranging 31-40 per annum during the past few years. The number of new drug approvals in 2011 (*n*=22) is the lowest in the last 12 years.

A list of selected 'new drugs' approved during 1999-2011 is presented in table 4. The list is categorized in terms of ATC classification. Some stereoisomers of existing molecules were also approved during 1999-2011. These stereoisomers included: R-sibutramine, S-amlodipine, S-metoprolol, R-ondansetron, S-pantoprazole, S-atenolol, S-etodolac and S-bupivacaine. It is worth noting that subsequent to their approval, some of the drugs were banned by the Indian drug regulatory authority. These banned drugs were Rimonabant, Rosiglitazone, Sibutramine, R-Sibutramine, Gatifloxacin (for systemic use), Tegaserod, Rofecoxib and Valdecoxib[5].

Table 4: A list of selected 'new drugs' approved during 1999-2011

A: Alimentary tract and metabolism
Fosaprepitant, Ilaprazole, Troxipide, Irsogladine, Sitagliptin, Exenatide, Ademetionine, Clebopride, Ondansetron, Rabeprazole, Palonosetron, Saxagliptin, Lafutidine, Ramosetron, Cinitapride, Voglibose, Vildagliptin, Cimetropium, Lansoprazole, Pantoprazole, Esomeprazole, Aprepitant, Rimonabant, Mebeverine, Itopride, Tiropramide, Caroverine, Racecadotril, Trimebutine, Rebamipide, Miglitol, Orlistat, Fenoverine, Metadoxine, Nateglinide, Paromomycin, Tegaserod, Balsalazide, Mosapride, Repaglinide, Rosiglitazone, Rifaximin, Levocarnitine, Granisetron, Pioglitazone, Octylonium, Glimepiride
B: Blood and blood forming organs
Dabigatran Etexilate, Cilostazol, Rivaroxaban, Prasugrel, Tranexamic, Enoxaparin, Fondaparinux, Dalteparin, Eltrombopag, Clopidogrel, Bemiparin, Camostat, Bivalirudin, Tirofiban, Triflusal, Eptifibatide
C: Cardiovascular system
Aliskiren, Ivabradine, Dronedarone, Ranolazine, Levosimendan, Telmisartan, Ambrisentan, Rosuvastatin, Ramipril, Nadolol, Perindopril, Bosentan, Chlorthalidone, Acipimox, Carvedilol,

Temozolamide, Nicardipine, Ivabradine, Eprosartan, Moxonidine, Nicorandil, Cholestyramine, Pitavastatin, Eplerenone, Olmesartan, Doxazosin, Imidapril, Metolazone, Bendrofluazide, Trandolapril, Fluvastatin, Ezetimibe, Fosinopril, Lercanidine, Nebivolol, Quinapril, Valsartan, Trapidil, Irbesartan, Candesartan, Pravastatin, Milrinone, Atorvastatin, Fenofibrate
D: Dermatologicals
Tacalcitol, Retapamulin, Luliconazole, Sertaconazole, Methoxsalen, Halometasone, Eberconazole, Sodium Hyaluronate, Eflornithine, Diflorasone, Acitretin, Trolamine, Pimecrolimus, Isotretinoin, Imiquimod, Azelaic Acid, Amorolfine, Tazarotene, Butenafine, Oxiconazole
G: Genito urinary system and sex hormones
Silodosin, Udenafil, Pentosan polysulfate Sodium, Naftopidil, Oxybutynin, Dapoxetine, Trospium, Darifenacin, Cabergoline, Apomorphine, Solifenacin, Dutasteride, Alfuzosin, Tadalafil, Mifepristone, Tamsulosin, Cyproterone, Raloxifene, Alprostadil, Sildenafil, Tolterodine
H: Systemic hormonal preparations, excl. Sex hormones and insulins
Deflazacort, Cinacalcet, Desmopressin, Ganirelix, Teriparatide, Nafarelin, Doxercalciferol
J: Antiinfectives for systemic use
Raltegravir, Azithromycin, Oseltamivir, Imipenem+Cilastatin, Doripenem, Fluconazole, Clindamycin, Caspofungin, Micafungin, Anidulafungin, Darunavir, Tenofovir Disoproxil, Nevirapine, Posaconazole, Amphotericin B, Abacavir, Valganciclovir, Maraviroc, Balofloxacin, Ribavirin, Atazanavir, Ertapenem, Zanamavir, Daptomycin, Cefditoren, Cefdinir, Pazufloxacin, Cefepime, Rifabutin, Prulifloxacin, Cefprozil, Cefetamet, Saquinavir, Tobramycin, Atazanavir, Tigecycline, Stavudine, Telbivudine, Gemifloxacin, Levofloxacin, Cefixime, Nelfinavir, Emtricitabine, Faropenem, Efavirenz, Didanosine, Entecavir, Adefovir, Linezolid, Voriconazole, Cefuroxime, Meropenem, Famciclovir, Valacyclovir, Aztreonam, Indinavir, Moxifloxacin, Gatifloxacin, Ganciclovir
L: Antineoplastic and immunomodulating agents
Crizotinib, Abiraterone, Fludarabine, Topotecan, Basiliximab, Daclizumab, Capecitabine, Trastuzumab, Rituximab, Temozolomide, Imatinib, Exemestane, Vinorelbin, Gemtuzumab, Thalidomide, Sirolimus, Bicalutamide, Cladribine, Anastrozole, Gemcitabine, Tacrolimus, Everolimus, Gefitinib, Erlotinib, Bortezomib, Fulvestrant, Paclitaxel, Pemetrexed, Sorafenib, Lapatinib, Sunitinib, Docetaxel, Glatiramer, Ixabepilone, Carmustine, Doxifluridine, Bendamustine, Decitabine, Trabectedin, Dasatinib, Temsirolimus, Miltefosine, Pazopanib, Nilotinib, Irinotecan, Temozolomide, Pirfenidone, Cytarabine, Cabazitaxel
M: Musculo-skeletal system
Nabumetone, Meloxicam, Rofecoxib, Celecoxib, Zoledronic Acid, Parecoxib, Valdecoxib, Risedronate, Aceclofenac, Ibandronic Acid, Diacerein, Etoricoxib, Strontium Ranelate, Eperisone, Lumiracoxib, Dexibuprofen, Lornoxicam, Oxaprozin, Etodolac, Cyclobenzaprine, Phenyramidol, Tizanidine, Tolperisone, Loxoprofen, Dexketoprofen, Amtolmetin Guacil, Febuxostat, Zaltoprofen
N: Nervous system
Sulpiride, Topiramate, Zuclopenthixol, Zolpidem, Tetrabenazine, Paroxetine, Venlafaxine, Moclobemide, Fluvoxamine, Olanzapine, Ropinirole, Oxcarbazepine, Citalopram, Bupropion, Donepezil, Mirtazapine, Reboxetine, Acamprosate, Fosphenytoin, Butorphanol, Quetiapine, Vinpocetine, Ziprasidone, Zaleplon, Divalproex, Sufentanil, Modafinil, Vinpocetin, Aripiprazole, Rizatriptan, Escitalopram, Entacapone, Atomoxetine, Duloxetine, Ziprasidone, Lamotrigine, Citicoline, Memantine, Tiagabine, Cabergoline, Zonisamide, Pregabalin, Levetiracetam, Pramipexole, Midazolam, Amisulpride, Desflurane, Etizolam, Edaravone, Varenicline, Eplerstat, Eszopiclone, Paliperidone, Milnacipran, Betahistine, Naratriptan, Desvenlafaxine, Dexmedetomidine, Methadone, Ropivacaine, Nicotine Polacrilex, Levosulpiride, Rasagiline, Ramelteon, Opipramol, Lacosamide, Armodafinil, Zotepine, Flupirtine, Tofisopam, Dosulepin, Eletriptan, Tiapride, Tapentadol, Asenapine, Eslicarbazepine, Iloperidone
P: Antiparasitic products, insecticides and repellents
Bulaquine, β-arteether, Nitazoxanide, Arterolane+Piperaquine, Artemether+Lumefantrine
R: Respiratory system
Bambuterol, Zafirlukast, Desloratadine, Ebastine, Poractant Alfa, Levocetirizine, Mizolastine, Montelukast, Tiotropium, Levosalbutamol, Rupatadine, Erdosteine, Levodropropizine, Ciclesonide, Doxophylline, Olopatadine, Fexofenadine, Acebrophylline, Ozagrel, Arformoterol, Fluticasone, Zileuton, Levocloperastine, Indacaterol, Acrivastine
S: Sensory organs
Trifluridine, Brimonidine, Apraclonidine, Loteprednol Etabonate, Bimatoprost, Unoprostone, Dorzolamide, Ibopamine, Travoprost, Epinastine, Pegaptanib, Bromfenac, Nepafenac, Flurbiprofen, Acetylcysteine, Difluprednate, Levobetaxolol, Tafluprost, Besifloxacin, Brinzolamide
V: Various
Iomeprol, Iobitridol, Meglumine gadoteric, Gadoversetamide, Gadobenate, Neotame, Lanthanum Carbonate, Sevelamer, Acesulfame Potassium, Deferasirox, Perflutren

DISCUSSION

The study identified total 1506 approvals by the DCGI from 1999 to 2011, the period under the study. An average rate of approval, per annum turns out to be 115.84 (Median approvals per year: 79; Range: 23-264). This number looks impressive. Of course one should not forget that the approvals included the drug products of the existing drugs for additional indications, additional dosage forms, additional higher or lower strengths, new salts and combination with other drug/s. In terms of dosage forms, about 2/3 of the approved drug products are meant for oral administration; about 1/4 are meant for parenteral administration and topical application. It is to be noted that as per ATC classification, the approved drug products are maximum in the group N (Nervous system). That is followed by group J (Antiinfective for systemic use), group A (Alimentary system) and group C (Cardiovascular). Each constitutes more than 10 per cent of the approved drug products. Even the 'new drug' entries are higher in these categories (in each group there are more than 10 per cent of approved 'new drugs'). In Group L (Antineoplastic and immunomodulating agents) also there are good numbers of 'new drug' entries. These approvals in the above groups reflect the use of drugs in the society.

It is important to look for the situation with the entry of the new molecules as approved 'new drug'. The approvals of newer molecules as drug during the period under study are comparatively lesser in number. Total of 448 'new drugs' are approved during the period from 1999 through 2011. Thus an average of 34.46 drugs is approved per year (Median new drug approvals per year: 36; Range: 22-53). This annual rate of approval of 'new drugs' in India in the present study is higher as compared to the US FDA data for ten year period from 2001 through 2010 (Mean: 22.9±5.36; Median: 21.5; Range: 17-36)[6]. However, the data of the past years show that during 1988-2002, the mean number of 'new drugs' approved in India was 26.4±9.5[7]. This rate appears lesser than what is observed in the present study. Of course there is overlapping of data of 4 years (1999 to 2002). This simply point outs the better performance of Indian pharmaceutical industry in recent past. The revised strategies of the pharmaceutical industry, better technical knowhow, multinational collaborations, improved economy of the country and realization of better marketing avenues in India may be the speculative factors for the observed performance. This is probably a reflection of the fact that the Indian pharmaceutical companies in general took the advantage of process patent law in India and introduced copycat drugs developed by the foreign multinational corporations (MNCs). The pattern of 'new drug' approval looks flattened around the years when patent policy change was introduced. In year 2011, there is a sharp decline in 'new drug' approvals, which is in line with the 'new drug' approvals in the developed market (in the United States, Mean 22.9±5.36; Median: 21.5; Range: 17-36)[8].

One of the concerns due to product patent is that the prices of drugs would rise. Because patent on a product would give a monopoly for the patent holder to decide the price of the product dimmed necessary to compensate the R&D expenses. However, to say that the market would be totally driven only by the patented products

may also not be correct. On an average, only 15 to 20 drugs enter the market every year globally and only a few of them are commercially successful. At the same time, each year patents for the earlier products expire. Hence, at a particular point of time only 5 to 10 percent of the drugs in the market may be under product patent protection and the rest of the market could still be in the generic category. Availability of the patent expired therapeutic equivalents would, automatically keep the prices of such new entities under control.

The new drug approvals data from the US FDA show that there is flat approval rate in past few years[8]. The reason for this flat approval rate over the time is that drug companies are not filing as many applications with FDA for new drug approval as they had in the past[8]. In Global economic slowdown, MNCs are cutting their R&D budget and reducing their employees. All these factors may lead to slowing of new drug development and approvals. One may expect that the trend of new drug approvals in India will now be similar to that in the developed markets. Most of the multinational pharmaceuticals companies (MNCs) have presence in India and they may try to introduce their patented drug products in India, simultaneously along with the introduction in the developed markets.

Another trend we observed in this study is that there is more interest in launching fixed dose combinations, stereoisomers and new dosage forms. As development of a 'new drug' is a lengthy process and very costly affair, the Indian companies are focussing in launching of fixed dose combinations, stereoisomers and new dosage forms of the existing products. The attempt is to differentiate the new product from the existing ones. This may be part of survival in the increasing competition amongst the drug-houses. Because of process patent in India before 2005, there are so many brands available in the Indian market for single drug molecule. It's not easy for the pharmaceutical companies to differentiate their brands from the competitors. Thus, to differentiate their product from the competitors some innovations are attempted. These attempts are resulting into the products mentioned above. Drug development is a risky, unpredictable and expensive process involving combination of scientific excellence and a thorough understanding of the business environment. Many Indian companies are shifting to contract manufacturing, outsourcing, contract research or tie-ins with MNCs. With the introduction of product patents, Indian companies will have to shift the area of focus from process development to developing new drug products, if not independently then at least, in the collaboration with MNC giants to make a beginning. Of course, there are number of confounding factors to take care of.

There is additional aspect about the fixed dose combination in Indian scenario. The grant of fixed dose combinations by different State Licensing Authorities (in India) has been a very contentious issue. There has been no uniformity in the different states as regards to grant of permission to manufacture such combinations. This has led to a situation where another State Licensing Authority grants a product not permitted by one State Licensing Authority[9]. This study included the fixed dose combinations approved by the DCGI office only. There is a possibility that our list doesn't include some fixed dose combinations available in the Indian market approved by different State Licensing Authorities.

There is a great scope for implementing all the rules and regulations, which would guide, monitor and control the activities of the providers of the healthcare system in the country and to find the means to bring the situation up to the international standards. Recommendations of Mashelkar committee[9] and establishment of the Central Drug Authority at the earliest, for control over manufacture, quality & supply of drugs are important from this angle. Besides approval of drug products there are number of issues related to healthcare system and availabilities of drugs. Comprehensive changes are needed in regulatory system to keep abreast with the changing trends in the industry with the objective of maintaining uniform parameters to produce quality drugs. Regulatory infrastructure needs to be strengthened to ensure good quality of products and check the production of spurious drugs.

India's population is just over 1.2 billion at present and projected to rise to 1.7 billion by 2050 and India will become the world's most populous country[10]. This projection shows that the demand of drugs will rise in coming years. There is a need, at national level to acquire an expertise in the field of R&D and to develop the technology to build up capacity in innovation and production of the drugs to ensure that essential drugs at affordable prices are available to the vast population. The R&D of new drugs should be in line with the country's healthcare needs. Further analysis on disease pattern and it's comparison with the pattern of new drug introduction would guide us to identify the right strategies to improve healthcare needs of India.

CONCLUSIONS

The results of this study confirm that there is a rising trend of approval for fixed dose combinations. The pattern of 'new drug' approval was flattened around the years when patent policy change was introduced. Nervous system (15.4%), antiinfective for systemic use (13.54%), alimentary tract and metabolism (12.74%) and cardiovascular system (12.35%) were top four ATC groups which received highest number of approvals.

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