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Review Article

THE CRAVE OF FIXED DOSE COMBINATION IN INDIAN MARKET

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ABSTRACT

The aim of the present retrospective works reveals the need of fixed-dose combination (FDC) in Indian market as per the Indian regulations. A combination drug most commonly refers to an FDC, which is a formulation including two or more active pharmaceutical ingredients combined in a single dosage form, which is manufactured and distributed in certain respective fixed doses. This review outlines the FDCs rationale, guidelines on data required for approval for marketing FDCs, marketing potential throughout the world. The safety of the combination drugs has to be thoroughly evaluated, and there are considerations for the drugs that are already in the market as individual or single-drug entity. However, the safety profile of the established drugs will alter when they are combined together. However, many of the irrational combinations are popular and widely prescribed by physicians in our country. This study provides a comprehensive analysis of the current markets for FDC products throughout the world and the market potential of promising drugs under development.

Keywords: Fixed dose combinations, Active pharmaceutical ingredients, Human immunodeficiency virus, Chronic obstructive pulmonary disease, World Health Organization, Non-steroidal anti-inflammatory.

INTRODUCTION

The development of fixed-dose combinations (FDCs) is becoming increasingly high either improving compliance or to benefit from the added effects of the two or more active drugs given together. They are being used in the treatment of a wide range of conditions and are particularly useful in the management of chronic conditions.

FDC drugs have been used for some time in certain therapeutic categories such as anti-hypertensives, although they were often reserved for second or third-line therapy. With the revolution in the survival rates of patients suffering from human immunodeficiency virus (HIV) infection that occurred with the implementation of fixed drug combination products for this indication, this delivery technology received a boost of confidence, as well as an influx of creative applications to other diseases.

"The global market for FDC drugs for leading diseases" analyzes products and applications of FDC drugs utilized in the treatment of cardiovascular diseases (hypercholesterolemia and hypertension), diabetes, infectious diseases (bacterial infections, *Helicobacter pylori,* acquired immune deficiency syndrome AIDS, HIV infection and tuberculosis), psychiatric disorders (depression and Alzheimer's disease [AD]) and respiratory diseases (asthma and chronic obstructive pulmonary disease [COPD]). Not included in this report are combination products used as oral contraceptives, combinations of the drug (such as a monoclonal antibody) and a radioactive component, or combination vaccine products. Furthermore, not included are over-the-counter (OTC) and prescription non-systemic FDC products.

The scope of this report is worldwide. The overview section provides a discussion of the history and advantages of FDC drug products. Described are the leading diseases for which FDC products are available or are projected to be introduced during the forecast period. This section also discusses the various types of products available or in development within the categories included in this report [1].

FDC for COPD

Decision resources, one of the world's leading research and advisory firms for pharmaceutical and healthcare issues, finds that the drug market for COPD therapies will become more fractured as several new agents reach the market over the next decade.

Two maintenance therapies currently dominate the COPD market Boehringer Ingelheim/Pfizer's Spiriva and GlaxoSmithKline's (GSK) Advair/Seretide/Adoair. In 2011, combined sales of these therapies constituted nearly two-thirds of the COPD market. As new therapies launch, they will erode the dominance of Advair/Seretide/Adair and Spiriva, and combined market share of these two agents will fall to 12% in 2021.

The pharmacor advisory service entitled finds that the market for COPD will increase from nearly $9 billion in 2011 to $13.3 billion in 2021 in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan. Growth in the market will be in part driven by uptake of a new drug class FDC inhalers containing a long-acting beta 2 agonist (LABA) and a long-acting muscarinic antagonist (LAMA) that will launch in 2014 and offer more potent bronchodilation than currently available treatments. In 2019, LABA/LAMA combinations are expected to become the sales-leading drug class in COPD and in 2021 they will capture more than 33% of the market share.

"Advair and Spiriva have dominated COPD treatment for a number of years, and although they will still be widely used, most interviewed experts are excited about LABA/LAMAs," said decision resources analyst Amanda puffer. "Thought leaders expect to use these combinations in COPD patients of all severities and think they will have a significant impact on the treatment algorithm" [2].

New York, May 31, 2012/PRNewswire/— Citeline, the world's leading research authority on pharmaceutical clinical trials, updates, and intelligence recently reviewed the results presented at the American Thoracic Society (ATS) conference held May 18-23, 2012 in San Francisco, CA. The strong competition to launch the next FDC blockbuster for COPD was of particular interest to reviewer Jennifer Stacey, Cite line's Analyst in autoimmune/inflammation.

In the absence of results from GSK and theravance's market-leading Relovair program, top COPD trials data presented at the conference include results from Novartis' Phase III NVA237 GLOW2 trial and final Phase II data from Boehringer Ingelheim's olodaterol mono-therapy program. Both drugs provided significant improvement in bronchodilation with once-daily dosing, and these studies supported the dose selections for their respective FDC trials. Mid-sized companies

almirall and Forest showed sustained success of their partnered aclidinium bromide drug program, while privately-held pearl therapeutics divulged eight clinical publications at ATS, revealing statistically significant efficacy results and future plans for their LAMA/LABA (glycopyrrolate+formoterol fumarate), PT003.

"The presentations at ATS this year provide further evidence of high competition to launch next generation FDC respiratory drugs. COPD has superseded asthma as the lead indication in the market race, most likely due to the Food and Drug Administration (FDA) new safety controls pertaining to limited use of all LABA-containing drugs in asthma, as well as the unmet need for improved therapies for COPD," states Ms. Stacey, "In addition, it appears that most companies are strategically conducting trials to launch their novel LAMA or LABA as mono-therapy in advance of the registration of the associated FDC product."

Despite the notable omission of pivotal Relovair trial data from this year's ATS proceedings, GSK and theravance continue to be the trailblazers in the race to launch the next generation COPD therapy through their partnership in two key FDC programs, Relovair (fluticasone furoate+vilanterol) and their LAMA/LABA combination (719+vilanterol). With the patent expiry of Advair in 2011 and the looming expiration of symbicort later this year, GSK has positioned itself as the front runner in capturing a large share of the future respiratory market with these two strong Phase III FDC drug programs and plans to submit regulatory Relovair applications for COPD in the US and Europe in mid-2012. However, several competitors are riding on their heels, including Boehringer Ingelheim, Novartis, Almirall/Forest, and the up-and-coming pearl therapeutics, with strong FDC candidates in their pipelines.

"Pearl Therapeutics is only in planning stages for their Phase III FDC program and is certainly the underdog among the current competition, but their innovative PT003 product had stellar Phase II data at ATS and they announced plans for PT010, a triple combination therapy of LAMA (glycopyrrolate), LABA (formoterol fumarate), and an inhaled corticosteroid, in one of their presentations," comments Ms. Stacey. "They will be an exciting company to watch as competitors in the FDC respiratory market race cross the finish line for novel inhaled therapies in COPD [3]."

"We are excited to present the first Phase III data for tiotropium+olodaterol FDC, which marks another important milestone in our goal of developing innovative therapies to address the unmet medical needs in COPD," said Professor Klaus Dugi, Chief Medical Officer, Boehringer Ingelheim. "Leveraging our extensive heritage and expertise in the Respiratory Therapeutic Area, Boehringer Ingelheim is expanding into further chronic respiratory areas, including rare diseases where few treatment options exist [4] (Table 1)."

The global anti-hypertensives market for FDC

The market is expected to witness comparatively slow growth with a compound annual growth rate (CAGR) of 1.2% between 2010 and 2017, to reach $32.6 billion in 2017. The steady increase in the hypertension and pulmonary arterial hypertension (PAH) prevalence population, and the use of FDC drugs will drive the growth of the anti-hypertensive's market in the future. The market for hypertension market is expected to slow down due to patent expiries of major blockbuster drugs. Recent and upcoming patent expiries of drugs are the only barrier to the global anti-hypertensives market. However, the expected launch of novel molecules with disease modifying characteristics and better safety and efficacy will drive the market in the forecast period [5].

Table 1: FDC recommended by USFDA and EU for COPD

Serial number	Brand name	Drug name	Indication
1	Adair	Fluticasone/salmetrol	COPD
2	Spiriva	Fluticasone propionate/salmetrol xonofoate	COPD
3	LAMALABA	Glycopyrolate+Formeterol fumarate	COPD
4	Breo ellipta	Fluticanazole furoate+Vilanterol	COPD

COPD: Chronic obstructive pulmonary disease, EU: European, FDC: Fixed dose combination, LAMA: Long-acting muscarinic antagonist, LABA: Long-acting beta 2 agonist, USFDA: United States Food and Drug Administration

The global anti-hypertensives market was estimated to be worth $29.9 billion in 2010, representing a CAGR of 5.8% between 2002 and 2010. The market is forecast to reach $33 billion by 2017 at a CAGR of 1.2%. The primary reason for the slowdown in the market growth is the patent expiries of major blockbusters in the forecast period. Drugs that are set to lose patent include Novartis' Diovan (2012), Sanofi's Avapro (2012), Novartis's Exforge (2012), Takeda/AstraZeneca's Blopress/Atacand (2012), Pfizer's Revatio (2012), Boehringer's Micardis (2014), United Therapeutics Remodulin (2014), Actelion's Tracleer (2015) and Daiichi Sankyo's Benicar (2016). These drugs together accounted for more than $20.6 billion in revenues in 2010. However, the market is expected to rise slightly after 2015 due to increased usage of FDC and the increase in prescription population on generics. The new FDC, which entered the antihypertensives market recently, are Exforge HCT, Tektuna HCT, Tekamlo, Valturna, Tribenzor, Twynsta, Edarbi and Amturnide. The current anti-hypertensives pipeline offers some promising novel products indicated for the treatment of hypertension and PAH such as SPP635, Actos, LCZ696, QT1571, ACT-293987, PS-433540, macitentan, and riociguat. However, the revenues that will be generated from these products are not expected to completely make up for the revenue losses due to patent expiries (Tables 2-4) [5-8].

FDC for the treatment of glaucoma

Alcon, the global leader in eye care and the division of Novartis, announced that the Committee for Medicinal Products for Human Use of the European Medicines Agency has issued a positive opinion for Simbrinza® eye drops suspension (brinzolamide 10 mg/mL and brimonidine tartrate 2 mg/mL) to decrease elevated intraocular pressure (IOP) in adult patients with open-angle glaucoma or ocular hypertension, for whom monotherapy provides insufficient IOP reduction [9].

Simbrinza® combines two medicines already approved for the treatment of elevated IOP into one multi-dose bottle, to be dosed with one drop

Table 2: FDC recommended by USFDA and EU for hypertension and hyperlipedimics

Serial number	Brand name	Drug name	Indication
1	Tekamlo	Alisidren; amlodipine	Hypertension
2	Tribenzor	Omlesartan medoxomil; amlodipine; hydrochlorothaizide	Hypertension
3	Exforge HCT	Amlodipine, valsartan, hydrochlorothiazide	Hypertension
4	Azor	Amlodipine; omlesartan medoxomil	Hypertension
5	Benicar HCT	Omlesartan medoxomil; hydrochlorothaizide	Hypertension
6	Azor Tablet	Amlodipine/olmesartan	Hypertension
7	Copalia HCT	Amlodipine/valsartan/ hydrochlorothiazide	Hypertension
8	Simcor	Naicin extended release; simvastatin	Dyslipidemias
9	Advicor	Niacin extended release; lovastatin	Dyslipidemias
10	Juvisync	Sitagliptin; simvastatin	Dyslipidemias
11	Caduct	Amlodipine besylate; atorvastatin calcium	Hypertension angina; dyslipidemias

EU: European, FDC: Fixed dose combination, USFDA: United States Food and Drug Administration

into the affected eye(s) twice daily. If approved, this FDC therapy will offer a simplified eye drop schedule and reduce the treatment burden for patients suffering from open-angle glaucoma or ocular hypertension (Tables 5-7) [10].

Obstacles to use of FDC

Formidable obstacles still prevent the widespread introduction of FDCs, including problems with bioavailability of one or more components [11], lack of regulatory quality control, and pressure from interest groups in some developing countries to maintain irrational combinations [12]. We briefly summarize some of the most important barriers.

Regulatory/pharmacological obstacles

Uncertainties regarding the quality of FDC formulations and their registration, and barriers to effective implementation in national programs, have limited the widespread use of FDCs. Bioavailability of individual components may change when put into combination with other components. For example, variable bioavailability of the tuberculosis drug rifampicin from solid oral dosage forms has been reported, whereas bioavailability problems with the isoniazid, pyrazinamide and ethambutol components of FDCs have not been encountered, presumably because of the much greater water solubility and more rapid rates of absorption of these latter drugs [13]. Hence, using FDC tablets with poor rifampicin bioavailability could lead directly to treatment failure and may encourage drug resistance. Other FDC components may have similar issues [14].

Table 3: FDC recommended by USFDA and EU for DM

Serial number	Brand name	Drug name	Indication
1	Juvisync	Sitagliptin; simvastatin	T2DM
2	Prandimet	Repaglinidine, metformin Hcl	T2DM
3	Januma	Sitagliptin; metformin Hcl	T2DM
4	Actoplus Met	Pioglitazone Hcl; metformin Hcl	T2DM
5	Ristfor tablet	Sitagliptin/metformin	Diabetes
6	ACTO plus met XR	Metformin/pioglitazone	Diabetes

EU: European, FDC: Fixed dose combination, T2DM: Type 2 diabetes mellitus, USFDA: United States Food and Drug Administration

Table 4: FDC recommended by USFDA and EU for HIV

Serial number	Drug name	Indication
1	Abacavir+Lamivudine	Antiretroviral
2	Didanosine+Lamivudine	Antiretroviral
3	Didanosine+Emtricitabine	Antiretroviral
4	Stavudine+Lamivudine	Antiretroviral
5	Tenofovir+Emtricitabine	Antiretroviral
6	Tenofovir+Lamivudine	Antiretroviral
7	Zidovudine+Lamivudine	Antiretroviral
8	Abacavir+Lamivudine+Efavirenz	Antiretroviral
9	Abacavir+Lamivudine+Nelfinavir	Antiretroviral
10	Abacavir+Lamivudine+Fosamprenavir	Antiretroviral
11	Abacavir+Lamivudine+ Fosamprenavir/Ritonavir	Antiretroviral
12	Didanosine+Lamivudine+Efavirenz	Antiretroviral
13	Stavudine+Lamivudine+Atazanavir	Antiretroviral
14	Stavudine+Lamivudine+Efavirenz	Antiretroviral
15	Stavudine+Lamivudine+ Lopinavir/Ritonavir	Antiretroviral
16	Stavudine+Lamividine+Nelfinavir	Antiretroviral
17	Stavudine+Lamivudine+Nevirapine	Antiretroviral
18	Tenofovir+Emtricitabine+Efavirenz	Antiretroviral
19	Tenofovir+Lamivudine+Efavirenz	Antiretroviral
20	Tenofovir+Emtricitabine+ Lopinavir/Ritonavir	Antiretroviral

EU: European, FDC: Fixed dose combination, HIV: Human immunodeficiency virus, USFDA: United States Food and Drug Administration

Pharma point AD – UK drug forecast and market analysis to 2022

Global Data has released its new Country report, "Pharma Point: AD – UK Drug Forecast and Market Analysis to 2022." There are no long-term effective therapies for AD, so this remains at the top of the list for unmet needs. While physicians agree that symptomatic therapies are relatively safe and effective, these therapies are still lacking because of they cannot maintain their effects and lack mechanisms that alter the course of the disease [15].

As in the other markets covered in this report, the patent expirations of the key marketed drugs will drive a reduction in the market until 2015; both Aricept and Reminyl lost market exclusivity in 2012, and Ebixa will come off patent in 2014. Arimenda, the FDC reformulation of two of the expiring medications, is expected to enter the market in the short term, but is not expected to make up for the sales lost by the patent cliff for Aricept and Ebixa.

Investment arguments

Domestic market growth to be muted for FDC

The Indian Pharmaceutical market in FY12 stood at Rs. 63,000 cr - more than double than in FY07. This market is estimated to grow at 15% CAGR up to 2020 driven by lifestyle diseases such as cardiovascular, diabetics and Oncology as has been the case in the past. FDC has grown its domestic revenues by 60% over FY07-FY12 while the market has doubled due to lack of strong brands in these fast growing segments. Market share is down to 1.2% from almost 1.5% in FY07. We expect FDC's domestic business to grow at higher single digits given stiff competition from MNC and leading domestic players [3].

Exports hold huge potential

Higher formulations exports with exports revenues at Rs. 84 cr in FY12 or twice that in FY06/FY07. Ophthalmic is a $18 billion market

Table 5: FDC recommended by USFDA and EU for TB

Serial number	Drug name	Indication
1	Rifampicin+Isoniazid+Pyrazinamide+ Ethambutol	Anti TB
2	Rifampicin+Isoniazid+Pyrazinamide	Anti TB
3	Rifampicin+Isoniazid	Anti TB
4	Isoniazid+Ethambutol	Anti TB
5	Thioacetazone+Isoniazid	Anti TB
6	Rifampicin+Isoniazid+Pyrazinamide	Anti TB
7	Rifampicin+Isoniazid	Anti TB

TB: Tuberculosis, EU: European, FDC: Fixed dose combination, USFDA: United States Food and Drug Administration

Table 6: FDC recommended by USFDA and EU for antiobesity

Serial number	Brand name	Drug name	Indication
1	Qsymia	Phentermine+Topiramate	Antiobesity

EU: European, FDC: Fixed dose combination, USFDA: United States Food and Drug Administration

Table 7: FDC recommended by USFDA and EU for glaucoma

Serial number	Brand name	Drug name	Indication
1	SIMBRINZA	Brinzolamide+ Bromonidine tartarate	Glaucoma

EU: European, FDC: Fixed dose combination, USFDA: United States Food and Drug Administration

globally - 1200 × FY12 exports for FDC. Of this, glaucoma is a $6 billion market where FDC has approvals from the UKMHRA and USFDA for key drugs. We estimate exports to grow at 25% CAGR over FY12-FY14 on a conservative basis.

Valuations and view

Revenues are likely to rise over FY12-FY14 Eat 11% CAGR with earnings growth of 12% CAGR. Valuations factor in these doubts on growth and allocation of cash, as well as concern of the negative impact of large cash balance on return on equity. Our recommendation on FDC is not based on a growth premise but on quality\Value that we see in the stock. We recommend a buy on FDC for a target of Rs. 125 based on 15 × FY13 estimated earnings per share. Upsides to the target are possible on clarity of use of cash.

FDC in India

FDCs should always be based on convincing therapeutic justification. Each FDC should be carefully justified and clinically relevant (e.g., in cases when each component of the FDC has several possible dosages, dosages that have shown benefit on clinical outcomes may be preferable).

Appendix VI of Schedule Y (Drugs and Cosmetics Rules 1945) specifies the requirements for approval for marketing of various types of FDCs. The same is further elaborated to provide a detailed guidance for industry [16].

Scope

These guidelines apply to manufacture/import and marketing approval of FDCs as a finished pharmaceutical product considered as a new drug as per Rule 122 (E) of Drugs and Cosmetics Act and Rules.

Drug control issues indian scenario [17]

The Indian drug control authority has issued notifications banning many FDCs. The principal notification under Section 26-A of the Drugs and Cosmetics Act, 1940, (prohibiting manufacture, sale and distribution of certain FDCs, which do not have any therapeutic justification or are likely to involve risk to the human being) banned 79-drug formulations from the year 1983 till date. Some examples are FDCs of vitamins with anti-inflammatory agents and tranquillizers, of anti-histamines with anti-diarrheals etc. It is an accepted fact that an FDC be treated as a new drug, because by combining two or more drugs, the safety, efficacy, and bioavailability of the individual active pharmaceutical ingredient (API) may change. As per the Drugs and Cosmetic Act, 1940, any new drug and the permission to market a drug is to be given by the Drugs Controller General of India (DCGI). As per rule 122 (E) of the Drugs and Cosmetic Rules, 1945, the same criteria holds good for US markets as well.

FDCs in the Indian scenario

More than one-third of all the new drug products introduced worldwide during the last decade were FDC preparations. The trend varied from country to country. In Japan, only 10% of the new products were fixed ration combinations, whereas, in European countries like Spain, it was up to 56%. However, such statistical data are lacking for the developing countries, although, the trend seems to be the production and prescription of FDCs. The World Health Organization (WHO) lists nearly 325 essential drugs, including only 19 of such drug combinations. Whereas, the national list of essential medicines has 354 essential drugs, including 14 drug combinations. FDCs available for the treatment of various ailments range from nutritional deficiency to cardiovascular diseases. Maximum FDC preparations comprise vitamins, cough suppressants, anti-diarrheal, iron preparations, antacids, analgesics, and tonics [18].

There are many popular FDCs in the Indian pharmaceutical market, which have flourished in the last few years. Medical experts world over have been expressing serious concerns over the marketing of increasing number of drug combinations by pharmaceutical companies, particularly in the developing countries. Some FDCs can impose unnecessary financial burden, increased adverse effects, as well as hospitalization, and decreased quality of life.

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The DCGI had given marketing approvals for 40 FDCs in January 2002. It is an accepted fact that an FDC be treated as a new drug, because by combining two or more drugs, the safety, efficacy, and bioavailability of the individual API may change. As per the Drugs and Cosmetic Act, 1940, any new drug and the permission to market a drug is to be given by the DCGI. As per rule 122 (E) of the Drugs and Cosmetic Rules, 1945, the same criteria holds good for US markets as well. WHO has made the following observations regarding the FDCs, as new fixed ratio combination products are regarded as new drugs in their own right [18].

FDCs are highly popular in the Indian pharmaceutical market and have been particularly flourishing in the last few years. The rationality of FDCs should be based on certain aspects such as [19]:

- The drugs in the combination should act by different mechanisms
- The pharmacokinetics must not be widely different
- The combination should not have supra-additive toxicity of the ingredients.

Most FDCs have the following demerits:

- Dosage alteration of one drug is not possible without alteration of the other drug
- Differing pharmacokinetics of constituent drugs pose the problem of frequency of administration of the formulation
- By simple logic, there are increased chances of adverse drug effects and drug interactions compared with both drugs given individually.

The recent 14th model list of essential drugs prepared by the WHO (March 2005) includes 312 formulation of which 18 are fixed dose drug combinations. WHO model list of Essential Drugs provides examples of some rational FDCs such as:

- Sulfamethoxazole+trimethoprim
- Antitubercular FDCs like rifampicin+isoniazid, isoniazid+ethambutol, etc.
- Ant parkinsonism FDCs like levodopa+carbidopa [19].

The drug utilization study of antimicrobial agents in medical intensive care unit of a teritiary care hospital shows the cefoperazone+sulbactam (J01DD62) 224 (30.8%) was the most common FDC noticed [20]. In India, a variety of non-steroidal anti-inflammatory drug (NSAID) combinations are available, often as OTC products. These combinations are an easy way to sell two drugs when one (or even none) may be needed for the patient.

Diclofenac sodium (DIC) is a synthetic NSAID, has been proved to be safe and efficacious drug in the treatment of a variety of inflammatory and rheumatoid disorders. Thiocolchicoside (THIO) is a muscle relaxant which has been claimed to possess GABA mimetic and glycinergic actions. It is used in the symptomatic treatment of painful muscle spasm. Combination of DIC with THIO in FDC was determined spectrometrically which shows the quality of FDCs and advancement in analytical technique for combination therapy [21].

The “combined” pills are marketed with slogans like “ibuprofen for pain and paracetamol for fever” and “ibuprofen for peripheral action and paracetamol for the central action.” It is indeed very unfortunate that the

medical fraternity in India has fallen prey to such gimmicks. The gullible patient then has to pay for the doctor's complacence in terms of extra cost and extra adverse effects. There is no synergism when two drugs acting on the same enzyme are combined. Thus combining two NSAIDs does not and cannot improve the efficacy of treatment. It only adds to the cost of therapy and more importantly, to the adverse effects and the 'muscle relaxants' in some of these combinations are of questionable efficacy.

Combinations of NSAIDs/analgesics with antispasmodic agents are also available in India. They are not only irrational but also could be dangerous. The antipyretic drug promotes sweating and thereby helps in heat dissipation. On the other hand, the anticholinergic antispasmodic drug inhibits sweating. Combining these two can result in dangerous elevation of the body temperature. Some such fixed drug combinations are now banned in India.

Over the years the Indian Drug Control Authority has issued banned notifications on many FDCs like analgin+pitofenone, vitamins B1+B6+B12, cyproheptadine+lysine, etc. But are these measures sufficient? Obviously not, since these notifications have not deterred manufacturers from coming out with new irrational FDCs. At this crucial juncture, when the global community, represented by WHO, is making an all-out effort to propagate the concept of essential drugs amongst consumers throughout the world, our official stance could be viewed as too meager. India, as the world's second most populous country, should demand a more rational approach and not pay mere lip service to the global campaign.

CONCLUSION

The Pharmaceutical market in India comprises combination drugs as 46% about Rs 70,000-crore. Today, when we read diabetes guidelines recommending early use of combination therapy, we tend to forget that Indian diabetologists have been using this form of treatment for over 40 years. Today, when the pharmaceutical industry celebrates the approval, by the FDA, of a FDC for diabetes, we do not realize that these combinations were the norm in India nearly half a century ago. The development and needs of FDCs plays a pivotal role in public health sector because of potential lower cost comparing to separate products. Simpler logistics and reduced development of resistance in case of antimicrobials. FDC therapy reduces poly pharmacy and pill burden, which improves patient compliance. Identifiable population group epidemiologically favors FDC. The rationality and therapeutic justification of all FDC's are the most controversial issue in current clinical practice. The knowledge about FDC's were lacking in resident doctors, which leads irrational prescription. The Indian laws have not been properly defined to grant marketing approvals of the FDC by state or central drug controlling authority. However, truly effective regulation equal to and necessary for India's major contribution to global drug manufacture will not happen without legislators with vision who see the need for a new drugs Act.

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