

Regulatory Status of Fixed Dose Combinations in India

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Abstract: Introduction: Fixed dose combinations is a combination of two or more different active ingredients in a fixed ratio of drugs.

More than one drug is used frequently for the treatment of either single or multiple comorbid conditions. Many of the fixed dose combinations available are bizarre.

Ex: fixed dose combinations of Quinolones and Nitroimidazoles [Norfloxacin + metronidazole, Ciprofloxacin + Tinidazole] have not been recommended in any standard books.

Aim: To study about the regulatory status of fixed dose combinations in India.

Materials and Methods:

This is the time trend analysis of regulatory status of FDCs in India from the year 1983 – 2018.

Information gathered from various articles published in journals at PubMed.

Data collected from the CDSCO official website regarding approved fixed dose combination formulations which were banned by Health Ministry of India.

Results: Though there was a proposal of banning 294 drugs irrational FDCs in the year 2007 and 344 combination drugs in the year 2016, couldn't have been implemented due to failure of drug control regulatory authorities of both central and state.

In 2018 with the recommendations of Prof C.K. Kokate committee and Drug Technical Advisory Board, the 328 irrational FDCs were banned.

Conclusions: FDCs should ensure the safety and effectiveness of the drug formulations.

Transparency and accountability of regulatory authorities must be improved.

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I. Introduction

A combination of two or more pharmaceutical ingredients in fixed ratio in single dosage form is called fixed dose combination drugs.

If a combination of drugs to be called fixed dose combination, it must full fill this below criteria:

1. The drugs should act by different mechanism of action
2. Pharmacokinetics should not be wide different
3. The combination should not produce additive side effects

Presently for a patient for single or multiple comorbidities more than one drug is prescribed. Irrational use of combination of drugs are bizarre. Most importantly antimicrobials, irrational use leads to drug resistance. As per WHO bulletin 2016 approximately 7, 00,000 deaths per annum globally related to anti-microbial resistance (AMR).

II. Aim

To study about the regulatory status of fixed dose combinations in India.

III. Materials And Methods

This is the time trend analysis of regulatory status of FDCs in India from the year 1983 – 2018. Information gathered from various articles published in journals from PubMed. Data collected from the CDSCO official website.

According to the Amendment of drugs act 1982- India gained the power to ban manufacture and sales of certain drugs and irrational fixed dose combinations.

In 1983 JULY 1st time Government of India issued Gazette notification to ban several drugs and FDCs after due consideration based on observed adverse drug reactions.

In 2005 MARCH WHO released 14th model list of essential drugs which includes 18 FDCs out of 312 medicines but, Indian market has innumerable combination drugs.

Many times International drug regulators expressed concerns about the quality of fixed dose combination drugs in India. Many fixed dose combination drugs were considered unsafe and even dangerous. Irrational use of antimicrobial fixed dose combination drugs leads to antimicrobial resistance (AMR). WHO bulletin 2016 MAY clearly says the approx. death toll 7lacs due to antimicrobial resistance which would climb to 10 million in the next 35 years.

In the year 2007-CDSCO banned 294 fixed dose combination drugs from sale. As these drugs Instead of getting approval from Drug Controller General of India (DCGI), many FDCs got approval from State authorities, which is not legal. Manufacturers obtained a stay from Madras high court. The matter remained unresolved.

IN 2011 Central Drugs Standard Control Organisation (CDSCO) was examined by the department related parliamentary standing committee on health and family welfare and in 2012 issued a report saying multiple deficiencies in Central Drugs Standard Control Organisation (CDSCO). Few and important among them are,

1. CDSCO acted more as a facilitator for the drug industry than protector of consumer.
2. Expert opinion regarding approval of new drugs were drafted by manufacturers and asked experts to put signatures.
3. Experts acted unethical while giving opinion about drugs.
4. Drugs unlawfully approved.

In the year 2016- Government of India banned 344 FDCs adding 5 more to the previous list, report submitted by the Prof C.K. Kokate committee. Immediately drug manufacturing companies moved to various courts against the decision seeking stay on the ban. Delhi high court noted that the decision was made by the advice of the technical committee instead of consulting Drug Technical Advisory Board (DTAB).

In the year 2017 DECEMBER- Health ministry challenged the stay on ban in Supreme Court, directed DTAB to decide the fate of these drugs.

In the year 2018 SEPTEMBER the Health ministry through a gazette notification, prohibited 328 FDCs considering the recommendations of DTAB and the expert committee. Different pharmaceutical companies seek Delhi high court to challenge the decision of MoHFW to stop manufacture, distribution, sales with immediate effect. Delhi high court directed that no coercive steps to be taken against the sale of 328 FDC drugs that were banned but are still available in the market. Ordered the companies to give the batch numbers of the stock available in the market.

Reasons Mentioned by Drug Technical Advisory board (DTAB) for Ban Fixed Dose Combinations:

1. There is no advantage therapeutically
2. May risk to human beings
3. These FDCs in the market neither boost any advantage over individual drugs
4. Anti-microbial FDCs make human body resistant to treatment

Tip of the iceberg:

The All India Drug Action Network (AIDAN) is a civil society group working on safety and access to medicine , one of the petitioners in the supreme court said in the statement. "The banned FDCs account for about Rs 2500 crores is the only tip of an iceberg" estimating the market for usage, problematic FDCs in India is atleast 1/4 of the total pharmaceutical market valued of Rs 1.3 trillion.

Fate of banned drugs:

It has become a biggest task for DCA officials to make sure the FDCs are withdrawn from medical shop. Till now in A.P., Drug control authority (DCA) officials could recalled the drugs worth of Rs 20 crores across the state. Could not gather the information about other states. Nowhere mentioned in the official websites of drug control authorities.

Some of the important questions still in the minds of public.

Is still banned drugs available in the market?

Is India becoming the drug dumping yard?

How drug manufacturers got permission for clinical trials for FDCs when it is not fulfilled the criteria to be a FDC?

IV. Conclusion

1. FDCs should ensure the safety and effectiveness of the drug formulations.
2. Irrational the death toll rate can increase to 10 million and the economic burden can rise to approx. 100 trillion US dollars
3. Transparency and accountability of regulatory authorities must be improved.
4. Support should be provided to CDSCO in terms of planning, information system and skilled personnel.
5. Government should frame and implement strict laws for manufacturers, wholesalers and retailers of pharmaceutical industries to safe guard the public health.
6. Manpower of DCA of states should be increased to meet the needs.
7. Continuous medical education programmes should be conducted for the government and private practitioners to enlighten about the banned drugs and the reasons behind it by the senior faculty of Pharmacology department.
8. Create the public awareness about what drugs and why they were banned.
9. FDCs which are not rationale and with no therapeutically justification should be banned.
10. Drug regulatory authorities and govt should not encourage unethical practices of drug manufacturers including FDCs

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