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Review on Market Withdrawal of Molecular Entities

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Abstract:

The number of single dose drugs as well as fixed dose combination drugs are banned in other countries but they have manufacturing, marketing and distribution in india.

Drugs are made to save lives and not causes deaths. Every drug has some side effect if the dose ofthe drug is correct ,then it can be avoided. Some drug / adverse effects can be reduced by another drug . hence, doctor prescribed medication is safer then self medication. Banned drugs have moreadverse / side effects. Doctors should stop prescribing banned drugs and due to less demand manufacturer will not produce such drug. As well as the government should make strict laws against the peoples involved in manufacturing and selling of banned drugs. Government should be ordered to dump this chip drug in proper manner. And also, India's pharmacovigillance effort hasto be scaled up rapidly. People should say stop selling banned drugs.

Keywords: combination drugs, banned drugs, side effects, pharmacovigillance

Introduction:

The drugs are chemical or synthetic substance which used for diagnosis, treatment mitigation , prevention of a disease , disorder & otherwise enhance physical or mental well being. Drugs or medicines may be withdrawn from commercial market because of risk to patient, but also becauseof commercial reason. (e.g., lack of demand and relatively high production cost). Were risk or harms is the reason fir withdrawal ,this will usually have been prompted by unexpected adverse effect that were not detected during phase 3 clinical trials i.e. they we're only made apparent frompost marketing surveillance data collected from the wider community over longer periods of time.

The main objective of this review is to create awareness and knowledge regarding banned / harmfuldrugs / drug combination in India.

Drugs are chemical that change the way of persons body works. If you are sick and had to take drug prescribed by doctor it will make you gel well soon. Medicines are legal drugs, meaning doctors are allowed to prescribed them for patient, stores can sell them, and people are allowed to

by them. but's it is not legal, or safe, for people to use this medicines any way they want or to buythem from people aho are selling them illegally. Illegal drugs aren't good for anyone's.this drug damage the brain,heart,and other important organs such illegal drugs should be banned. Drugs have to pass from different phase of clinical trials before they are introduced into the market. Firstly they undergoes animal testing and then in human beings during clinical trials. during this different phases of efficacy as well as safety profile of the drug tested. But yet some adverse effects of drugs appear after their usage in the general population. It identifies unidentified ADRs, drug safety issue and risk benefit comparisons among medications belonging to different therapeutic classes. Banned drugs are those drugs which are not allowed to intake because they could artificially improve their performance and shows various adverse effects more than therapeutic effects, use or production of these drugs are strictly controlled or prohibited via prescription.

Some drugs may cause adverse effects only when combined with particular drugs. This adverse effect are detected though a process of regular monitoring after the drug is released called pharmacovigillance. If the adverse effect outweigh the benefits, or if the drug are is ineffective, the country may banned the drug and company recall that batch many spurious drug that have beenbanned or withdraw under restrictions in other countries, but continued to be sold in India. The pharmaceutical companies are playing with the lives of thousands of people who are not aware. of harmful effects of the drugs they sell. In such cases, a number of single drugs as well as fixed dose combinations have been banned for manufacturer, marketing and distribution in India. Indiais dumping ground for banned drugs. India is one of the few countries that export huge amount of banned drugs to other countries. Due to competition to become rich, many defaulters pharmaceuticals have been set up and growing in every direction there are poor provisions on check and control of spurious drugs in Indian market.

Even a large number of population takes medicines and drugs without prescribing a doctor whichcan be dangerous. More and more banned medicines are finding their way in india. this list is not limited to drugs that were ever approved by the FDA. Some of them (for example,lumiracoxib , rimonabant , tolrestat , ximelagatran , and ximelidine)were approved to be marketed in europe buthad not yet been approved for marketing in the US, when side effects became clear and their developers pulled them from the market. Some drugs in this list were never approved for marketingin the US or Europe. A drug is banned on the basis of risk versus benefit ratio evaluated through post marketing surveillance and adverse drug reaction reporting system. Drug misuse and abuse are major health problems harmful drugs are regulated according to classification systems that purport to relate to the harm and risks of each drug.

List of drugs withdrawn from the country particular year and its adverse effects:

Drug	Withdrawn	Country	Remarks
Zimelidine	1983	Worldwide	Risk of Guillain–Barré syndrome, hypersensitivity reaction, hepatotoxicity[3][64][65] banned worldwide.[66]
Ximelagatran (Exanta)	2006	Germany	Hepatotoxicity[14]
Xenazoic acid	1965	France	Hepatotoxicity.[3]
Vincamine	1987	Germany	Hematologic toxicity.[3]
Valdecoxib (Bextra)	2004	US	Risk of heart attack and stroke.[2]
Trovafloxacin (Trovan)	1999–2001	European Union, US	Withdrawn because of risk of liver failure[2][3]

Troglitazone (Rezulin)	2000	US, Germany	Hepatotoxicity[2]
Triparanol	1962	France, US	Cataracts, alopecia, ichthyosis.[3]
Triazolam	1991	France, Netherlands, Finland, Argentina, UK Others	Psychiatric adverse drug reactions, amnesia.[3][63]
Triacetyldiphenolisatin	1971	Australia	Hepatotoxicity.[3]
Tolrestat (Alredase)	1996	Argentina, Canada, Italy, others	Severe hepatotoxicity[3]
Tolcapone (Tasmar)	1998	European Union, Canada, Australia	Hepatotoxicity[3]
Ticrynafen (Tienilic acid)	1980	Germany, France, UK, US Others	Liver toxicity and death.[3]
Thioridazine (Melleril)	2005	Germany, UK	Withdrawn worldwide due to severe cardiac arrhythmias[61][62] Continues to be available in Russia.
Thiobutabarbitone	1993	Germany	Kidney injury.[3]
Thenalidine	1963	Canada, UK, US	Neutropenia[3][60]
Thalidomide	1961	Germany	Withdrawn because of risk of teratogenicity;[59] returned to market for use in leprosy and multiple myeloma under FDA orphan drug rules
Tetrazepam	2013	European Union	Serious cutaneous reactions.[58]

Terodiline (Micturin)	1991	Germany, UK, Spain, others	Prolonged QT interval, ventricular tachycardia and arrhythmia.[3]
Terfenadine (Seldane, Triludan)	1997–1998	France, South Africa, Oman, others, US	Prolonged QT interval; ventricular tachycardia[2][3]
Temazepam (Restoril, Euhypnos, Normison, Remestan, Tenox, Norkotral)	1999	Sweden, Norway	Diversion, abuse, and a relatively high rate of overdose deaths in comparison to other drugs of its group. This drug continues to be available in most of the world including the US, but under strict controls.
Temafloxacin	1992	Germany, UK, US, others	Low blood sugar; hemolytic anemia; kidney, liver dysfunction; allergic reactions[2][3]
Temafloxacin	1992	US	Allergic reactions and cases of hemolytic anemia, leading to three patient deaths.[2]
Tegaserod (Zelnorm)	2007	US	Risk for heart attack, stroke, and unstable angina.[2] Was available through a restricted access program until April 2008; returned to market in 2019.
Suprofen	1986–1987	UK, Spain, US	Kidney damage.[2][3]
Suloctidil	1985	Germany, France, Spain	Hepatotoxicity.[3]
Sulfamethoxypyridazine	1986	UK	Dermatologic and hematologic reactions.[3]
Sorivudine	1993	Japan	Drug interaction and deaths[50]
Efalizumab(Raptiva)	2009	Germany	Withdrawn because of increased risk of progressive multifocal leukoencephalopathy[12]
Adderall XR	2005	Canada	Risk of stroke [1] The ban was later lifted because the death rate among those taking Adderall XR was determined to be no greater than those not taking Adderall
Alatrofloxacin	2006	Worldwide	Liver toxicity; serious liver injury leading to liver transplant; death.[2
Alclofenac	1979	Uk	Vasculitis, Rash.[3]

The government has decided to prohibit manufacturing and sell of this medicine because they were found to be “irrational” without any therapeutic efficiency and use also in some cases there were concerns about misuse of such medicines considered unsafe for mass consumption. The health ministry has approved the ban order with immediate effect. A fixed dose combination (FDC) is one that contains two or more drug combined in a fixed ratio of doses and available in single dosage form. Health ministry has to release list of all banned drugs and it should be available easily to all outlets, all media, explore all names of the drugs banned. Health experts

say many unapproved formulations and FDC's are sold antidepressant and psychotic condition segment. Industry estimates suggest the move is likely to impact pharmaceutical sales to the tune of around Rs 1,500 crore For ensuring safety and efficacy of medicines, the health ministery has banned around 350 fixed dose combination drugs (FDC) drugs that were widely available in the market till now. These medicines include FDCs based on codeine, used in popular cough syrups like phensedyl and forex.

Complete new list of banned fixed dose combination drugs in 2016 :

- FDC of Aceclofenac + paracetamol + Rabeprazole
- Nimesulide + Diclofenac
- Nimesulide + cetirizine + caffeine
- Nimesulide + Tizanidine
- Paracetamol + Diclofenac + Famotidine
- Paracetamol + Phenylephrine + caffeine
- Naproxen + Paracetamol
- Tamsulosin + Diclofenac
- Heparin + Diclofenac
- Paracetamol + Cetirizine + Caffeine
- Diclofenac + Tramadol + Chlorzoxazone
- Dicyclomine + paracetamol + Domperidone
- Omeprazole + Paracetamol + Diclofenac
- Paracetamol + Pseudoephedrine + Cetirizine
- Azithromycin + Cefixime
- Amoxicillin + Dicloxacillin
- Ofloxacin + Nitazoxanide
- Clindamycin + Telmisartan
- Telmisartan + Metformin
- Ammonium citrate + vitamin B12 + Folic acid + Zinc sulphate
- Levothyroxine + Pyridoxine + Nicotinamide
- Benfotiamine + Metformin
- Thyroid + Thiamine + Riboflavin + Pyridoxine + Calcium pantothenate + Tocopherylacetate + Nicotinamide
- Ascorbic acid + Menadione sodium bisulfite + Rutin + Dibasic calcium phosphate + Adrenochrome mono semicarbazone
- Phenylephrine + Chlorpheniramine + paracetamol + Bromhexine + Caffeine
- Clotrimazole + Beclomethasone + Lignocaine + Ofloxacin + Acetic acid + Sodium methylparaben + propyl paraben.

Health ministry of India finalized that if any drug banned by two or more countries and it is still being marketed in India, they may possibly remove the drug from the indian market after proper examination or appropriate action will be taken. The ministry of health and family welfare had constituted an expert committee under the chairmanship of prof. Ranjit Roy chaudhury to formulate

policy and guidelines for approval of new drugs, clinical trials and banning of drugs. Theexpert committee submitted its report to the ministry of health and family welfare. Unacceptably large number of formulations, around 60,000 to 85,000 are banned by the committee.

Many of these medicines should not have been allowed to reach the market in the first place. Thecommittee asked to remove drugs which should never have been allowed to reach the market is being marketed. Many of these drugs are inherently unsafe and potentially hazardous. They do notappear in any textbook of medicine or pharmacology; nor do they find a place in the market of any country. Expert committee also recommended that if the drug is already in the market but twoor more countries remove the drug from their market on grounds of efficacy and safety, then the national drug regulatory agency should consider the possibility of removing the drug from the Indian market as well. It has been decided that if two or more countries remove a drug from their market on grounds of efficacy and safety, then the continued marketing of the drug in the country will be considered for examination and appropriate action.

Reason for ban :

1) Likely to involve risk to human beings
2) There are safer alternative available in the market
3) Found to have no therapeutic justification
4) Drug which is banned due to some serious toxic effects, adverse effects, adverse drug reaction, side effects are detected though a process of regular monitoring after the drug is released into the market.

-Drugs undergo rigorous or clinical trial testing before they are introduced into the market.Thedrug efficacy as well as safety profiles are tested.

The adverse effect of drugs is detected by regular monitoring after the drug released called pharmacovigillance.

Adverse drug reaction are officially described as A response to a drug which is noxious & unintended, & which occurs at dose normally used for prophylaxis, diagnosis or theropy of disease or for modification of physiological function [12]

In India the highest authority is drug controller general of India which extends the approval ofany drug or banned drug.

- **Drug control strategy:-**

-Present drug control efforts utilize several techniques in attempt to achieve their goal ofeliminating illegal drug use:

-Disrupting the market for drugs

-Prevention efforts that relay on community activism , public information campaigns to educatethe public on the potential dangers of drug use.

-Law enforcement efforts against elements of the supply chain through surveillance & undercoverwork [13]

Conclusion:

Before egrouse test passing in manufacturing development then after a service of quality control process only a drug can be released into market.

Large numbers of drugs are banned by most of European countries but still they are easily availablein indian market. Long term use

of such medicines can put negative impact on human health in various ways by damaging liver, kidney or any other organ, depression, blood pressure fluctuations etc. A ban is needed to protect the public's health and the quality of health care. A ban will require self-examination by the public, health care professions, pharmacist and the health care policy community. As vigilant citizens of this country, you need to keep your eyes and ears open and watch out for the kind of drugs we or our loved ones consume. India and Indians need to wake up before it is too late.

Drugs are designed to be life savers doctors should not prescribe these banned drugs pharmacist should up to date regarding drugs & their usage .

The marketing monitoring screening carefully reduces number of problems useful drugs in developed as ADR's in banned drug and subsequent licening.

To stop the use of banned drugs, what is need is the cumulative effort by doctors , pharmacists , researchers & manufactures along with the invol vemerct of strict & vigilant regulatory authorities.

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