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A Critical Analysis Study of Pharmacological and Clinical Information Provided in Drug Package Inserts Based on Drugs and Cosmetics Rules Guidelines

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ABSTRACT

Introduction:
Drug package inserts are officially approved documents provided along with the drugs by the drug marketing company. They act as an important source of information about the drug for both patients and physicians, which helps in proper administration and improving the safe use of medications. The pharmacological and clinical information presented in them for its consistency and completeness were analyzed in this study.

Materials and Methods:
The drug package inserts were collected and analyzed for the pharmacological and clinical information, based on the headings under Section 6.2 & Section 6.3 mentioned in Schedule D of Drugs and Cosmetics Act and Rules, 1945. The drug package inserts that were analyzed in this study included different drug formulations and drugs belonging to different systems.

Results:
This study shows that the generic name, the brand name of the drug, its active ingredient, therapeutic uses, dosage form, and manufacturer details are present in all the package inserts (100%). But details about safety and precautions are given only in about 90%. Information about pharmacokinetics, pharmacodynamics, pharmaceutical particulars, and the antidote for drug overdose are missing in many package inserts.

Conclusion:
From our study, we conclude that a majority of the package inserts provide adequate details regarding key information. However, we recommend mentioning the approximate cost of the drug, references for the information provided in it, along with the Toll-free number of the Pharmacovigilance Programme of India (PVPI) for reporting adverse drug effects.

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Introduction

Advancement in the field of modern medicine has resulted in the development of many new drugs for the management of different diseases. Once a new drug is developed and its efficacy is established in clinical trials, marketing and selling of the drug by pharmaceutical companies become important. The companies spend about one-third of their sales revenue on the marketing of their products. The importance given by the companies for marketing is so much that they spend twice the amount in marketing their drugs than that spent for research and development of new molecules(1).

The various marketing techniques used by pharmaceutical companies for drug promotion include visits of the medical representatives to the hospitals, providing free drug samples to the physicians, drug package inserts, direct to consumer advertisements, drug promotional advertisements, conducting and sponsoring of scientific meetings, symposiums, conferences, continuing medical education (CME) programs, and promotional trials (2).

Since these Drug Promotion Activities are highly informative and provide details regarding the product's chemical name, generic name, brand name, its pharmacological parameters, pricing, therapeutic claims, and the references to support these claims, they are generally accepted in the health care system. Moreover, the availability of new drugs is of little value unless the prescriber is aware and updated with the scientific information to use it safely and effectively.

According to WHO, these promotional activities and claims need to be truthful, the information provided should be reliable, updated, informative, balanced, and should be substantiated with adequate and necessary references (3). The physician's role is very important, and he should respond to these promotional activities in an ethical, responsible, and sensible manner. Prescribing information leaflets or Drug Package inserts are official documents accompanying the drugs provided by the manufacturers. They are considered to be nonpromotional in nature since they are available as inserts along with the drug package. They act as an important source of information regarding the safe usage and proper administration of drugs for the patients and are expected to contain all the necessary details. Because of the availability of the internet and advancement in information technology, patients can easily access the details about their medications. But the authenticity and reliability of such drug information obtained are questionable. Hence providing the required details in package inserts will help to improve the patient's compliance with the drug. They are also an important source for physicians to know about the newly approved and marketed medications. In India, 'The Drugs and Cosmetics Act (1940) and Rules (1945) govern the concept of drug package inserts. The Labelling and packaging information of drugs of Schedule D (II) of Section 6 lists the headings based on which the information in the package insert should be provided. The objective of this study is to analyze the pharmacological and clinical information presented in "Drug Package Inserts" for its consistency and completeness based on the Drugs and Cosmetics Act and Rules.

Materials and Methods

The drug package inserts for this study were collected from pharmacy stores and clinics in Chennai during the period between April 2020 and August 2020. Most of the tablets, capsules, injections, syrups, suspensions, creams, lotions, ointments had an accompanying package insert, while some did not come with a drug package insert. All the drug package inserts available in the pharmacy were collected, analyzed, duplicates were identified and excluded from the study. The remaining Drug Package Inserts were studied and evaluated for the pharmacological and clinical information, which were analyzed based on the headings mentioned in Schedule D of Drugs and Cosmetics Act and Rules, 1945(4). "Section 6.2" of this Act and Rules mandates that the information must be in 'English' language. It should provide important clinical information of the drug like posology and method of administration, therapeutic indications, contraindications, any special precautions and warnings, any drug interactions, contraindications in pregnancy

and lactation, effects on the ability to use machines or drive, undesirable effects/adverse effects and any antidote available for overdosage.

"Section 6.3" mandates pharmaceutical information on the list of excipients, incompatibilities, and information regarding shelf life. In addition to the above details in the Drug Package Inserts, the presence of other desirable details like cost, references, and extravagant claims was studied. The data were entered in an Excel sheet, and statistical analysis was done. The results were expressed as percentages.

Results

A total of 610 drug preparations were collected, which included different generic drugs, different brands of the same generic drug, and different dosage forms of the same generic drug. Of the 610 preparations, 540 had drug package inserts (88.52%), while 70 (11.48%) did not have package inserts. The 540 Drug Package Inserts included drugs commonly prescribed by the doctors and sold in the pharmacy on a valid prescription order. They were evaluated for the pharmacological and clinical information, which was analyzed based on the headings mentioned in Section 6 of Schedule D of Drugs and Cosmetics Act and Rules, 1945.

The drug package inserts that were analyzed in this study included different drug formulations like oral, injectables, topicals and their percentage is represented in Figure-1. The analyzed drugs were classified based on the different systems, whose percentage is shown in Figure-2.

This study shows that 100% of the package inserts analysed contain basic information like Generic & Brand names of the drug, its active ingredient, therapeutic uses, dosage form, and manufacturer details. (Table-1). More than 90% of the package inserts give details about the common adverse drug reactions, Precautions & Contraindications, and their use in Special populations. Major interactions and details of adjuvants/ excipients are mentioned in 80% But certain key information like Shelf life (63%), antidote for drug overdosage (34%) and pharmacokinetic, pharmacodynamic, and pharmaceutical particulars of the drug (68%) are found missing in a majority of drug package inserts. None of the drug package inserts make any extravagant claims. They do not mention the references for the information provided and do not indicate the approximate cost of the drug. (Table-1).

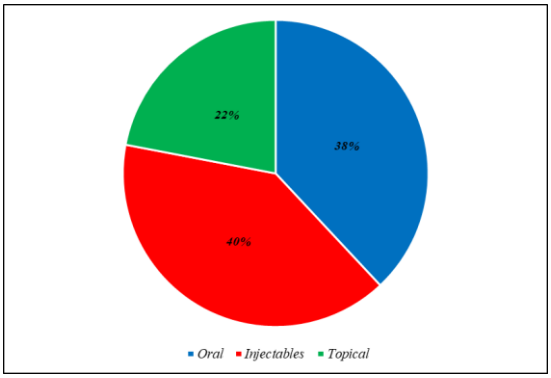

Fig 1: Package Inserts Analysed- Formulations

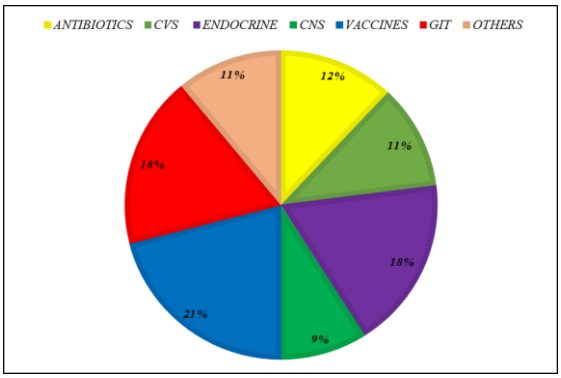

Fig 2: Package Inserts Analysed-Systems

Table 1: Presence of Various Parameters in Package Inserts Expressed In Percentage

Pharmacological and Clinical parameters	**Percentage**
Generic name of the drug	100
Brand name	100
Active ingredient	100
Therapeutic uses	100
Dosage form	100
Manufacturer Details	100
Shelf life	63
Excipients/Adjuvants	86
Adverse drug reaction	94
Precautions	96
Contraindications	91
Special population	91
Major interactions	82
Pharmacokinetics, Pharmacodynamics, pharmaceutical particulars	68
Antidote for Overdosage	34
References	0
Cost	0
Extravagant claims	0

Discussion

This study shows that 100% of the package inserts are having basic information like Generic & Brand names of the drug, its active ingredient, therapeutic uses, dosage form, and manufacturer details.

Regarding the details about safety and precautions, this study shows that more than 90% of the package inserts give details about the common adverse drug reactions, Precautions & Contraindications, and their use in Special populations (Table-1). Major drug interactions and details of adjuvants/ excipients are mentioned in more than 80%. Previous similar studies have also reported that information on the safe and appropriate use of medications was not uniformly provided on the package inserts and important information regarding drug's safety and efficacy are missing in the package inserts marketed in India (5,6). In another study done with scoring systems for the information given in package inserts, it was observed that only 79% of package inserts scored more than 50% (7). This study shows that the package inserts are missing some key information. The antidote for the drug overdose is mentioned in only 34% of the package inserts, probably because most of the drugs do not have an antidote and their overdosage is managed symptomatically. It also exposes that the pharmacokinetic, pharmacodynamic, and pharmaceutical particulars of the drug are given in only 68%. The shelf life of the drug is provided in only 63% of inserts which also includes the mentioning of shelf life as "refer to the carton" referring to the manufacture and expiry date printed on the drug packages and labels (Table-1).

This finding is similar to the study by Deepak Ramadas et al in which the authors concluded the necessary relevant information to the safe and effective use of the drug was not mentioned consistently in the analyzed package inserts (8). In another study, Shivkar mentioned that although the information in them has improved in the last decade, certain clinical information is missing and incomplete (9). Because of this incomplete and missing information, surveillance of these package inserts for uniformity and completeness would be beneficial for both patients and prescribers (10). This study reveals that none of the drug package inserts had extravagant claims. This is in contrast to Drug Promotional Advertising (DPA) materials which use phrases like "remarkably safe", "best-proven choice" as shown in a study on Indian DPAs (11). Because of these claims, physicians think these promotional advertising materials serve only to improve and increase the sales of drugs (12). Physicians do not think they are a dependable source of information while the technical language makes it difficult to use by the patients. Since package inserts are non-promotional, they can serve as a reliable source of information for the treating medical practitioners as well as the patients. [13] Hence we recommend that these drug package inserts can be given by the medical representatives to the physicians along with drug promotional materials during their promotional visit.

It will be a very good clinical material for the practitioners if references are given in package inserts to know the accuracy and validity of the information provided. Also providing the cost of the drug in package inserts will be useful for the prescribing doctors in assessing pharmacoeconomics and selecting a brand. We recommend these details can be added in package inserts as mentioned in an article by the author that "Indian drug package inserts need a revision."(14).

The Pharmacovigilance Program of India has provided a Toll-free number for the patients to report any adverse drug effects from anywhere across the country, any time of the day (15). Mentioning this number in the drug package inserts may be made mandatory to make it easier for the patients to report a suspected ADR.

The limitation of this study is that this study is done only with the drug package inserts available locally.

Conclusion

In our study, we conclude 100% of the package inserts provide adequate basic information, and more than 90% mention safety details like therapeutic uses, adverse effects, contraindications, warnings, and use in special populations. But the pharmacokinetic and pharmacodynamic

parameters are mentioned only in 68% of them and the rest are incomplete. We recommend surveillance of drug inserts for their completeness and uniformity. We also recommend mentioning the approximate cost of the drug in the package insert and add a list of references for the information provided in it. Mentioning the Toll-free Pharmacovigilance number of PVPI may be made mandatory in all the Package inserts since this will be very useful for the surveillance of ADRs (16).

Conflict of Interest

The authors declare they have no competing interests.

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