

Analysis of Package Inserts of Drugs Utilized in a Tertiary Care Hospital

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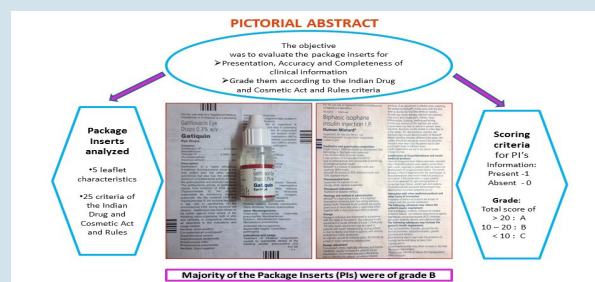
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ABSTRACT

Aim: To evaluate the Package inserts (PIs) for presentation, accuracy, completeness of clinical information and grade them according to the scores obtained. **Material and Methods:** An observational study conducted by the Department of Pharmacology, Sri Devaraj Urs Medical College from March to August 2014. PIs were analyzed for five leaflet characteristics and for 25 criteria listed by the Indian Drug and Cosmetic Rules, 1945. Each criteria was scored for presence of information as '1', absence as '0'. Total score of >20 was graded as 'A', 10-20 as 'B' and <10 as 'C'. Data was expressed as percentage. **Results:** Three hundred and sixty three PIs were analyzed. Considering the quality and texture, 80.2% were categorized as good and 19.8% as bad. All PIs were legible. Generic names were used in 99.2%. Content of active ingredients, indication for use were listed in 96.9% and 99.2% respectively. Posology details were mentioned in 97.2% and contraindications were given in 91.5% PIs. Undesirable effects were listed in 92.6%. Manufacturer's name and address was provided in 88.1%. PI with grade A, B and C were 10.2%, 83.8% and 6.1% respectively. **Conclusion:** Majority of the PIs were of grade B which suggests that most of the relevant information was mentioned except few criteria.

Key words: Information tool, Package insert, Rational prescribing, Posology, Generic name.

PICTORIAL ABSTRACT



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INTRODUCTION

Package insert (PI) is a document provided along with drug, it is also known as prescription drug label or prescribing information.¹ This provides the patient complete information in terms of the purpose, benefits and risks of the drug prescribed.² The PI is thus considered an important source of information for patients and health care providers in developing countries because of limited access to recent information about drugs.³

The prescribing physician plays an important role in providing drug information to most of the patients. An effective communication between the physician and the patients may not always be practically possible due to an inadequate doctor-patient ratio in India. A study has reported that low level of health literacy among patients and physician's inability to convey complete information about the drug, as barriers for patient-physician communication.⁴ Oral instructions are likely to be missed, misunderstood or forgotten. Hence, it is important that patients to certain extent require written information in order to use the drugs judiciously.⁵ In India, the concept of package insert is governed by the 'Drugs and Cosmetics Act (1940) and Rules (1945). The section 6 of Schedule D (II) of the rules lists the headings according to which information should be provided in the package inserts.⁶ A good PI should contain complete, approved, essential and accurate information about a drug.¹

Incomplete and incorrect product information may result in irrational prescribing leading to undesirable effects. Hence, this information tool must be constantly updated as and when relevant preclinical and clinical data is available.⁵ Therefore this study was carried out to critically assess the PIs using the criteria laid down by Indian Drug and Cosmetic Rules,

1945. PI were evaluated for presentation, accuracy, completeness of clinical information and they were graded based on their scores.

MATERIALS AND METHODS

An observational study was conducted by the Department of Pharmacology, Sri Devaraj Urs Medical College from March to August 2014. The protocol was approved by Institutional Ethics Committee. The study was carried out by collecting 363 package inserts from the pharmacy and wards of RL Jalappa Hospital and Research Centre.

All the package inserts were analyzed for five leaflet characteristics: Dimensions and layout, type of paper, absence of transparency, colour of paper and text, use of headings, pictograms or graphics. The PIs were also evaluated for the 25 parameters based on criteria laid down by Indian Drug and Cosmetic Rules, 1945: Legibility, approved generic name of active ingredients, content of active ingredient per dosage form, generic names of other ingredients, therapeutic indications, posology and method of administration, contraindications, special warnings and precautions, drug interactions, pregnancy and lactation, pediatric and geriatric indications, special conditions and contraindications, effect on ability to drive and use machines, undesirable effects, drug dose, over dosage, pharmacokinetic information, storage information, instructions for use and handling, shelf life, date on which information was last updated, name and address of manufacturer/distributor, provision of full information on request should be highlighted, retail price of the drug and references. Each criteria was scored for presence of information as '1', absence as '0'. Total score of >20 was graded as 'A', 10-20 as 'B' and <10 as 'C'. Descriptive statistics was used to analyze the data and expressed as percentage.

RESULTS

Three hundred and sixty three package inserts were analyzed. Considering the leaflet characteristics based on quality and texture, 80.2% (n=291) were categorized as good and 19.8% (n=72) as bad. Pictograms and graphics were present in 9.4% of PIs for better explanation of instructions. Average length and breadth were 22.35 ± 11.32 cm and 14.7 ± 7.49 cm respectively. White colour background and black text was used in 75.2%. The extent to which PIs followed the 25 criteria laid down by the Drug and Cosmetic Rules, 1945 is represented in Table 1.

Grade A suggests the PIs were good, B average and C poor category majority of them were graded B (Figure 1). Thirty seven PIs belonged to grade A, Ranbaxy laboratories limited had three PIs with grade A of which two had score of 24 and one had 23 (Figure 2). The PIs were categorized based on the scores obtained into grade B and C and maximum belonged to grade B (Figure 3). Package inserts were present in most of the cartons of tablets and injections (Figure 4) and highest was PIs with antimicrobials (Figure 5).

DISCUSSION

Package inserts belonging to different countries are approved by their regulatory bodies. Food and Drug Administration is the regulatory authority for United States, European Medicines Agency for Europe whereas in India it is the Ministry of Health and Family Welfare. Full prescribing information is submitted by the pharmaceutical companies as a part of the new drug application for marketing to the regulatory authorities.⁷ Once the application is approved, the information is accompanied with the drug in the drug cartons.

In India, the regulations for manufacture, distribution and sale of pharmaceutical products are present in Section 6 of Schedule D (II) of the Rules which relates to labelling, listing the headings according to which information should be provided in the package inserts. The headings

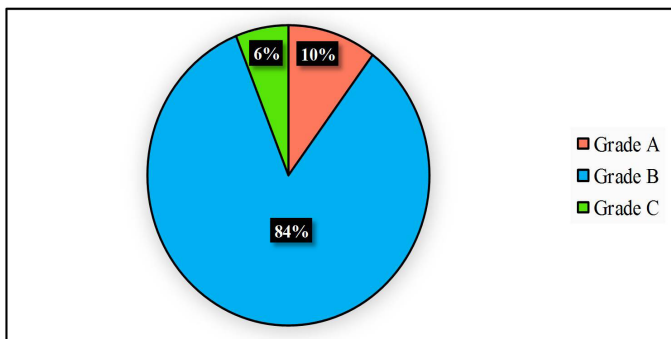


Figure 1: Grades of package inserts.

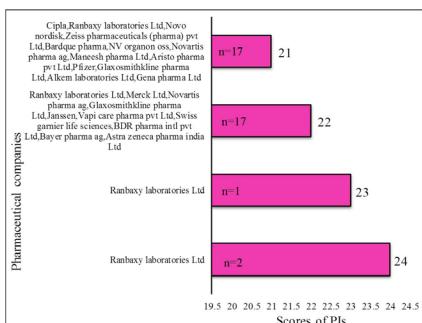


Figure 2: Package inserts that scored 21-25 (Grade A).

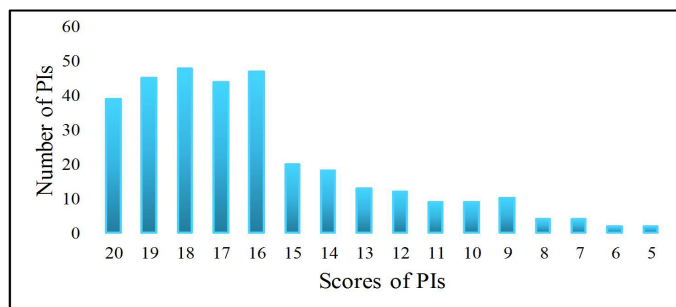


Figure 3: Package inserts categorized based on scores (Grade B and C).

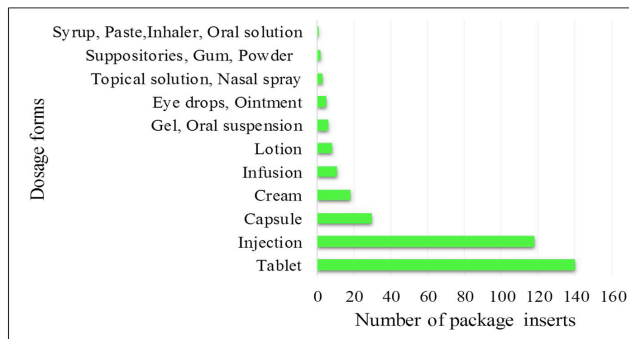


Figure 4: Package inserts based on the dosage forms.

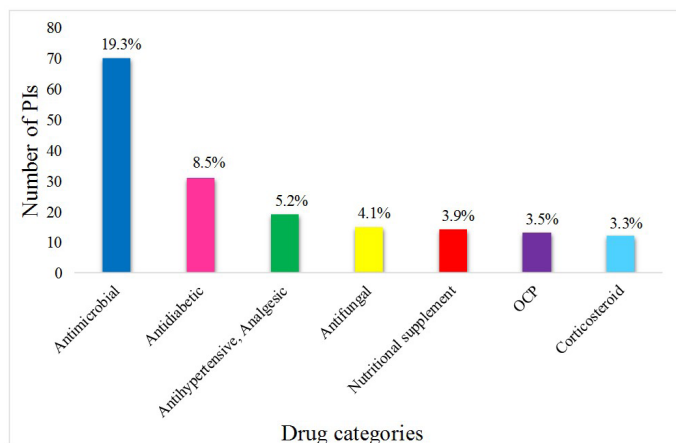


Figure 5: Categories of package inserts.

are grouped under two broad sections, Section 6.2 and 6.3 pertaining to importance of clinical use of the drug and pharmaceutical information respectively.⁶ We summed and included all the headings as 25 criteria for which the PIs were analyzed.

Leaflet characteristics of PI are important because no matter how good the information is, the paper should be presentable and have uniform characteristics. In our study, there was no uniformity in length and breadth and it was clumsy to handle an over-sized leaflet. There was no uniformity in font size which made it difficult for analyzing. The lack of uniformity in size, shape and font causes inconvenience not only to the prescribers but the patients as well. In a study regarding leaflet characteristics, it was reported that most of them were not satisfactory and the content in terms of readability, understanding should have been improved.²

Table 1: Package inserts that followed criteria laid down by Drug and Cosmetic Rules, 1945

Criteria	Mentioned (%)	Not mentioned(%)
Legibility (Yes/ No)	100	0
Approved generic name of active ingredients	99.2	0.8
Therapeutic indications	99.2	0.8
Posology and method of administration	97.2	2.8
Content of active ingredient per dosage form	97	3
Special warnings and precautions	93.4	6.6
Undesirable effects	92.6	7.4
Contraindications	91.5	8.5
Drug dose	89.3	10.7
Storage information	88.1	11.9
Name and address of manufacturer/distributor	88.1	11.9
Drug interactions	80.4	19.6
Pregnancy and lactation	79.1	20.9
Pharmacokinetic information	77.7	22.3
Over dosage	74.4	25.6
Pediatric and geriatric indications	65.8	34.2
Generic names of other ingredients	62.3	37.7
Instructions for use and handling	51.8	48.2
Special conditions and contraindications	32.5	67.5
Provision of full information on request-highlighted	30.9	69.1
Shelf life	24.5	75.5
Date on which information was last updated	18.7	81.3
Effect on ability to drive and use machines	17.6	82.4
References	9.4	90.6
Retail price of the drug	0	100

The quality and texture was good in 80.2%. The quality was assessed based on absence of transparency of the paper i.e. when the paper was placed on separate sheet with written text, a good quality paper would not reveal the text but bad would reveal it. The texture was assessed whether the written text on the reverse side of sheet is seen through while reading. Less than 10% had used pictograms and graphics. Pictorial representation should be increased since it adds value to the better understanding of the instructions from patient's point of view, especially from the rural areas.⁸ Information on PIs can also be made available in local languages as India is a country with many languages and most people are not familiar with English. In our study, only three PIs had information written in many languages but the disadvantage was that it had occupied a lot of space. All PIs used headlines to provide information, majority used white background and with black text.

Fuchs *et al* study did a survey on patients where majority (79.6% of all volunteers) said that they "always" read the PIs, 19.3% read "sometimes" and only 1.1% "never" read them.⁹ Gupta VK *et al* study also had similar result where majority i.e. 58% of all medical students read the PIs.³ This indicates the need for patient oriented PIs which provide the necessary information needed by common man. Fuchs *et al* study also ranked the criteria in the order of importance which is therapeutic indications, dosage instruction, ingredients, appropriate precautions for use, special warnings, contraindications, interactions, possible adverse drug reactions, therapeutic group, hints for application errors, application form and quantity of the drugs, storage, manufacturer, date of the last update.⁹ In our study, most (80%) of the PIs fulfilled the above criteria but only

18.7% mentioned the date of last update (Table 1). Mentioning this is important so that the patient's and physician's trust will be increased for the drug prescribed.

In addition, we have also analyzed the generic names of other ingredients, use in pregnancy and lactation, pediatric and geriatric indications, pharmacokinetic information, provision of full information on request, shelf life, date on which information was last updated, effect on ability to drive and use machines, references and retail price of the drug (Table 1). The last five criteria were mentioned in less than 25% of PIs. Details about effects of the drugs in the special conditions and driving are needed to avoid harm to patients. Information on shelf life is important as the drug that has passed its shelf life may still be safe for consumption but its quality cannot be assured and can lead to poor control of diseases like diabetes mellitus and hypertension. It is also important to list the inactive ingredients, such as sodium salts or artificial sweeteners because patients may be allergic to them. Contact details in case of any query should always be available. Retail prices have not been mentioned in any of the PIs, it would be beneficial for the patient if it is quoted.

We have observed that PIs were not provided with all the medications, it should be made mandatory. The PI can have an impact on the usefulness of drug usage by patients as it is seen only after receiving the medication.¹⁰ PIs are currently viewed as a legal formality rather than an effective tool for guidance.¹¹ Providing accurate and complete information about precautions, adverse effects, will promote rational use of medications.

There should be stringent rules to ensure that the pharmaceutical companies follow the regulatory guidelines regarding the structure, format of the PI so that there are no discrepancies in the 25 criteria. Therefore the requirement presently is to refine the contents of the PIs to make them complete, reliable and up to date. This can be a step forward for ethical and effective distribution of healthcare services in our society.

CONCLUSION

Majority of the PIs were of grade B which suggests that most of the criteria of the Drugs and Cosmetic act were met but the ultimate aim of all pharmaceutical companies should be to have Grade A quality package

inserts. The PI should be made mandatory and strict guidelines need to be implemented for uniformity of leaflet characteristics. Fulfilment of 25 criteria needs to be encouraged for propagation of knowledge and patient care.

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CONFLICT OF INTEREST

The author declare no conflict of interest.

ABBREVIATIONS USED

PI: Package Insert.

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