Original articles

ANALYTICAL EVALUATION OF DRUG PACKAGE INSERTS

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ABSTRACT

Introduction: *Package inserts are officially approved documents accompanying the drug which intends to provide information on safety and effectiveness of the product. This information is in accordance to country specific regulatory guidelines. It serves as a source of information to both users and prescribers. Hence the information incorporated has to be optimal to avoid medication errors.*

Objectives: *Evaluate the package inserts for completeness of information according to heading mentioned in Section 6.2 and 6.3 of schedule D of Drug and Cosmetic Rule, 1945.*

Methods: *Package inserts were collected from five pharmacies on request over a duration of 1 month and were analysed for the completeness of information according to Section 6.2 and 6.3 of schedule D of Drug and Cosmetic Rule, 1945. Information if present under the defined header, was scored one and zero if not. Total score of each header was calculated by adding the score from the individual package insert.*

Results*: 80 package inserts were included in the study. None of the reviewed package inserts contained all the headers as required by the Drugs and Cosmetics Act. Total 16 headings were evaluated under both Section 6.2 and 6.3, highest value for the presence of heading were 15 out of 16 headers. That shows the best value of compliance was 93.75%.*

Conclusion*: Present study encountered incompleteness of information in the package inserts. It is, therefore recommended that regulatory body should strengthen rules and regulations for the pharmaceutical companies to increase the compliance of adequacy of information in their package inserts to ensure rationale, effective and safe use of medicines.*

Keywords: Drug package inserts, Drug and Cosmetic Act, Prescribing information

Introduction

A drug package insert (prescribing information or patient information leaflet or prescribing drug label) is a document given along with the prescription or over the counter medication.[(1)] With increasing awareness and growing literacy in the community, the trend regarding the safety issues and healthcare is also changing. In the present digital era, it is a common practice among the consumers to refill their medication without the consultation of the prescribing doctors. As these drug dispensing facilities are available on one's door step, it is of even more importance to disseminate specific and complete information regarding the

marketed products. Package insert is one such mode by which the gap between user(consumer) and the health care service provider can be minimalised This would ultimately reduce the number of adverse drug reactions resulting from medication errors.

In India, the concept of drug package insert is governed by The Drugs and Cosmetics Act (1940) and Rules (1945).[2] The pharmacological information of the marketed product, which is provided as the drug package insert, is directed towards prescribers only. Keeping this into consideration, this study was designed to evaluate the presentation and completeness of available drug package inserts of commonly used drugs in India.

Method

This observational cross sectional study was conducted at Department of Pharmacology, AMC MET Medical College & Sheth LG General Hospital, Ahmedabad after the approval of the Institutional Review Board. The drug package inserts of commonly used drugs like antimicrobials, antihypertensives, antacids and non-steroidal anti-inflammatory drugs were collected from pharmacy stores located in five different areas of Ahmedabad over a period of 1 month. The duplicate package inserts (same drug, formulation, and company) were identified and excluded. The remaining package inserts were included in the study and analysed for the presentation and completeness of clinical information.

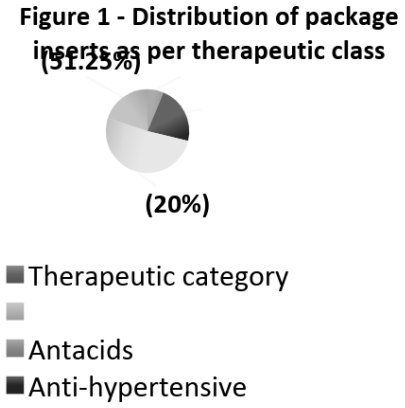
The clinical information included in the package inserts were analysed according to the headings mentioned in "Section 6.2 and 6.3" of Schedule D of Drugs and Cosmetics Rules, 1945. The Drugs and Cosmetics Act (1940) and Rules (1945) governs the concept of package insert in India. In Section 6 of Schedule D (II) of the Rules, 'Section 6.2' mandates that the package insert must be in English and must include information on therapeutic indications; posology and method of administration; contraindications; special warnings and precautions; drug interactions; contraindications in pregnancy and lactation; effects on ability to drive and use machines; undesirable effects; and antidote for overdosing. 'Section 6.3' directs pharmaceutical information on list of excipients; incompatibilities; shelf life as packaged, after dilution or reconstitution or after first opening the container; special precautions for storage; nature and specification of container; and instruction for use/handling.[3,4](Table 1)

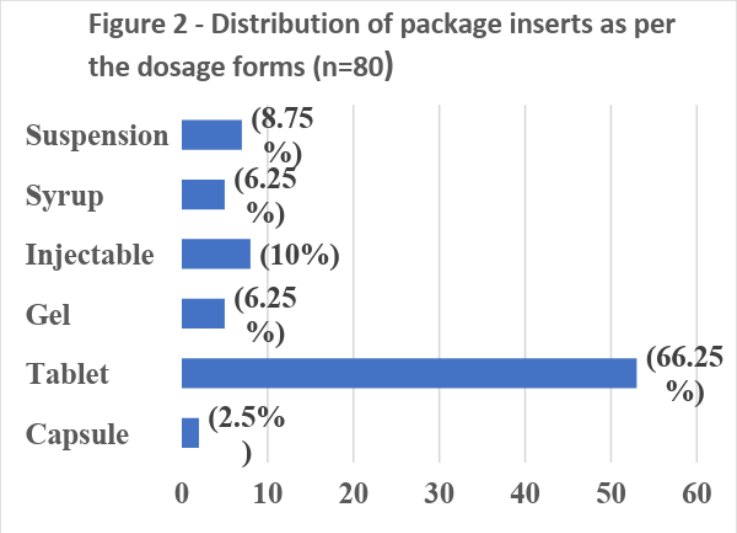
Table 1 – Schedule D of the Drugs and Cosmetics Rules (1945)	
Section 6.2	Section 6.3
Posology and method of administration	List of excipients
Contraindication	Incompatibilities
Special warning and precaution	Shelf life as package for sale
Interaction	Shelf life after dilution or reconstitution
Pregnancy and lactation	Shelf life after opening the container
Effects on ability to drive, if contraindicated	Special precaution for storage
Undesirable effects	Nature and specification of container
Antidote for overdosing	Instruction for use/handling

If the information was mentioned under relevant heading, score of one was given otherwise score of zero was assigned. The total score for each heading was them calculated by adding the score from individual drug package inserts. Final scores were expressed as absolute numbers and percentages.

Results

A total of 86 package inserts were collected from pharmacies during the study period. Of these, 06 duplicate inserts were excluded and remaining 80 were included for further analysis. The classification of drug package inserts as per the indication and dosage form is given in the Figure 1 and 2,respectively.





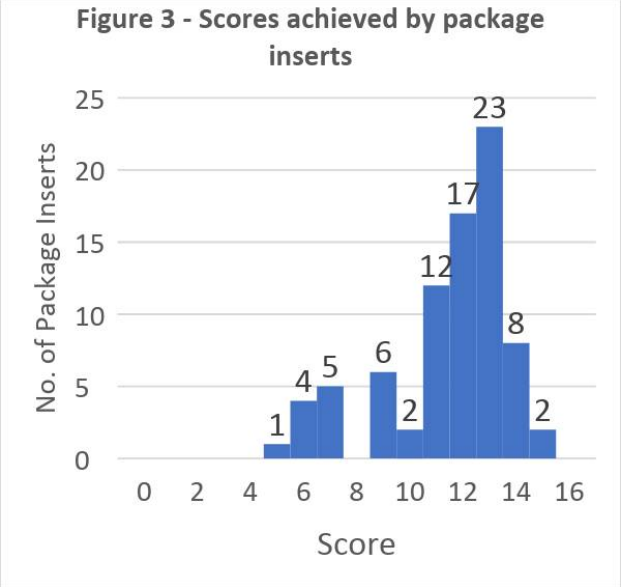
Analysis of data presented as per Section 6.2 and 6.3 is given in Table 2 . None of the reviewed inserts contained all the sections as required by the Drugs and Cosmetics Act.

Table 2 – Results of analysis of package inserts

Serial no.	Section 6.2	No. of package inserts (N=80)/ (Percentage)
1	Posology and method of administration	67(83.75%)
2	Contraindication	69(86.25%)
3	Special warning and precaution	57(71.25%)
4	Interaction	56(70.00%)
5	Pregnancy and lactation if contraindicated	68(85.00%)
6	Effect on ability of drive and operate machines	17(21.25%)

7	Undesirable effects/side effects	63(78.75%)
8	Antidote for overdose	67(83.75%)
Serial no.	**Section 6.3**	**No. of package inserts(N=80)/ (Percentage)**
9	List of excipients	79(98.75%)
10	Incompatibilities	06(07.50%)
11	Shelf life	11(13.75%)
12	Shelf life after dilution/reconstitution	07(08.75%)
13	Shelf life after opening the container	23(28.75%)
14	Special precaution for storage	80(100%)
15	Nature and specification of container	80(100%)
16	Instruction for use/handling	59(73.75%)

A total of 16 headings were evaluated mentioned under both Section 6.2 and 6.3. Maximum score of 15 was observed in 2 inserts whereas the minimum score encountered was 5, observed in only 1 insert; 23 package inserts had a score of 13 as shown in Figure 3. That shows the best value of compliance was 93.75%.



In therapeutic information, indications for use were present in 99% of package inserts. Posology and method of administration, and antidote for overdosing were present in 84% of the inserts. While 79% of the total inserts analysed had not mentioned the effect on ability to drive or use machines, if contraindicated. In pharmaceutical information, special precaution for storage and nature and specifications of container were represented in at least 80% of the inserts. Instruction for use and handling were mentioned in 73.75% of the inserts. Additional information, apart from that mentioned under section 6.2 and 6.3, were mentioned as clinical pharmacology, information update date, paediatric - geriatric use, clinical trials, mechanism of action. Food drug interaction, name and address of manufacture and provision of full information on request highlighted.

The shelf-life and incompatibilities were present only in 13.75% and 7.50% of inserts respectively. Variations in the layout of inserts varies from one company to other pharmaceutical company. All the inserts were legible.

Table 3 – Additional information in drug package inserts		
Serial no.	**Additional information**	**No. of package inserts(N=80)/ (Percentage)**
1	Clinical pharmacology/ mechanism of action	56(70.00%)
2	Information update date	26(32.50%)
3	Paediatric use	49(61.25%)
4	Geriatric use	30(37.50%)
5	Clinical trials	07(08.75%)
6	Pharmacokinetics	33(41.25%)
7	Name and address of manufacture	78(97.50%)
8	Provision of full information on request highlighted	30(37.50%)
9	Retail price	00(00%)
10	References	00(00%)

Discussion

The package insert is a good source of information for the users as well as the health care providers. Each country or region has its own administrative authority that regulates drugs and provides the information that consumers receive with their prescriptions. In India, it is the Central Drugs Standard Control Organization (CDSCO) Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India who monitors the import, manufacturing, sale and distribution of drug. The package insert follows a standard format which ensures safe and effective use of the drug by providing accurate, specific, complete and timely updated information in an easily comprehensible manner.

The results in our study shows up to 93.75% compliance in regards to the presence of important headings stated in the Sections 6.2 and 6.3 of Schedule D of Drugs and Cosmetics Rules, 1945 as when compared to the 71% compliance reported by Kalam et al. Under the section 6.3, list of excipients was present in majority (98.75%) of the inserts analysed which is higher than the that reported by Shivkar et al.[6] On the other hand, the posology and method of administration, contraindication, special precaution and undesirable/side effects warning was present in 83.75%, 86.75%, 71.25% and 78.75% of package inserts which is lower than the that reported by Shivkar et al.[6]

When correlated with the results of other such similar studies in regards to the headers mentioned for analysing the package insert, the vital information like drug interactions, pregnancy and lactation if contraindicated was noted in 70% and 85% respectively, which is quite similar to the that reported in studies by Shivkar et al and Solanki et al, [6,7] but slightly lower when compared to the study reported by Sudhamadhuri et al and Kalam et al.[8,9] However information on antidote for overdosage and effect on ability to drive was present in 83.75% and 21.25% respectively, which is more than that reported by Kalam et al.

As the consumers tend to refill their prescription without consulting the doctor, information under the heading ‘instructions for use/handling’ is of marked importance. Instructions for use/handling was mentioned in about 73.75% of the inserts, which is more than those reported by Sudhamadhuri et al, Kalam et al, Ramdas et al and Makbool et al, [8,9,10,11] Information

on storage, nature and specification of container was mentioned in 100% of package inserts, which is higher than the results reported by the studies earlier. The additional information present in the package inserts analysed under the heading of clinical pharmacology, clinical trials, pharmacokinetics and update date were encountered in 70%, 08.75%, 41.25% and 32.50% respectively, which is quite higher than that noted in Shivkar et al.[6] The information regarding the retail price and references were not mentioned in any of the inserts analysed, which was similar to that reported by Makbool et al.[11] The results of this study show higher percentage of presence of headings under pharmaceutical information compared to the study conducted by Sudhamadhuri et al and Ramdas et al. [8,10]

Conclusion

Package inserts are the source of information to the end users and hence are vital source of information for effective and safe use of drug. Awareness of this information also helps in increasing the patient compliance to treatment. The present study concluded that though major information is presented by the pharmaceutical companies in the package inserts, there are certain vital information like that on shelf life, incompatibilities and literature evidence from clinical trials been missed out. To ensure completeness of information, regulatory bodies should strengthen the policy of approval of product information documents in order to increase the compliance and uniformity of information mentioned in them.

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Ethical approval: The study was approved by Institutional Ethics Committee

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