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ANALYSIS OF COMPLETENESS OF DRUG PACKAGE INSERTS AVAILABLE IN PHARMACIES OF CENTRAL INDIA

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INTRODUCTION

Accurate and reliable drug information is essential for safe and effective use of marketed products. Incomplete and incorrect product information may promote irrational prescribing and may have serious consequences, including disability and death .The primary source of drug information is a Package Insert (PI). Drug package insert is the bedrock of methods used to inform people about their medicines. It is a printed leaflet that contains information based on regulatory guidelines for the safe and effective use of a drug. It is also known as prescription drug label or prescribing information. A good PI contains the approved, essential and accurate information about a drug. It is written in a language that is not promotional, false or misleading. It is evidence-based and is updated time to time as relevant pre-clinical and clinical data becomes available.[1] 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 PIs. The 'Section 6.2' mandates that the PIs must be in 'English' and provides information regarding therapeutic indications; posology and methods of administration; contraindications; special warnings and precautions; drug interactions; contra-indications in pregnancy and lactation; effects on ability to drive and use machines; undesirable effects; and antidote for overdosing. The 'Section 6.3' mandates 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.[2]

Regulatory requirements for drug package inserts or leaflets vary across the nations. United States-Food and Drug Administration (US-FDA) and European Medicines Agency (EMA) amend their regulations governing the content and format of labelling for drug products from time to time.[3] In India the regularity authority is Ministry of Health and Family Welfare, Government of India. The pharmaceutical companies submit the full prescribing information as a part of the new drug application for marketing. Once the application is approved by the regularity authorities, the information is accompanied with the drug in the package.[4]

India has an inadequate doctor: patient ratio. Thus, the accessibility of trained prescribers, for the entire Indian population, is difficult. An effective communication may not always be practically possible between the prescribers and the patients and so a well crafted PI could serve as an effective guide to help the patient be aware about the medication he has been subjected to. Also, with the tremendous growth of the science of Pharmacology and Pharmaceutics in recent times, a well designed package insert could serve as an effective tool to guide the prescribers, making the vast relevant information easily accessible and to decrease the medication/administrating errors and thus adverse events. Hence PIs are effective sources of information not only to the patients and/or paramedic staff, but also aid in updating the knowledge of the prescribing physicians.

Thus, our study was carried out to assess the presentation, completeness and accuracy of the information provided in the currently available package inserts for 200 different drugs in India according to the section (sec.) 6.2 and 6.3 of schedule D of Drug and Cosmetic Act, 1940 and to grade them according to the scores obtained.

MATERIAL AND METHODS

1. Collection of PIs

It is a cross sectional, observational study. A total of 100 PIs were collected from various pharmacies located in various parts of Nagpur on request, over a period of four weeks in the month of March 2015.

2. Analysis of content of PIs

PIs were scored based on criteria laid down by Indian Drug and Cosmetic Rules, 1945 under section 6.2 and 6.3 of schedule D.

3. Analysis as per Section 6.2 and 6.3 criteria

The PIs were analyzed based on the following criteria

1. Legibility.
2. Approved generic name of active ingredients.
3. Content of active ingredient per dosage form.
4. Generic names of other ingredients & list of excipients
5. Therapeutic indications.
6. Posology and method of administration.
7. Contraindications.
8. Special warnings and precautions.
9. Drug interactions.
10. Pregnancy and lactation.
11. Pediatric and geriatric indications.
12. Special conditions and contraindications.
13. Effect on ability to drive and use machines.
14. Undesirable effects.
15. Drug dose.
16. Antidote for Over dosage.
17. Pharmacokinetic information.
18. Storage information. Nature and specification of the container
19. Instructions for use and handling.
20. Shelf life: i) Shelf life in the medical product as packed for sale

ii) Shelf life after dilution or reconstitution according to direction

iii) Shelf life after first opening the container

21.Date on which information was last updated.

22.Name and address of manufacturer/distributor.

23. Provision of full information on request should be highlighted.

24. Retail price of the drug.

25. References.

4. Scoring and grading of PIs[5]

A total score of 25 was assigned to each PI, based on the above mentioned 25 criteria. Presence of information was scored as '1' and absence was scored '0'. Total score was also expressed in percentages.

- Score >20 graded as 'A';
- Score of 10-20 graded as 'B',
- and < 10 as 'C'.

RESULTS

Among the 200 PIs collected, 32 were repeated and not considered for the analysis in the study. Hence, total of 168 PIs were analyzed. On analysing the PIs, it was found that presentation of information was not uniform and it was difficult to locate and retrieve information easily due to lack of common layout and heading. Moreover, the package inserts were of different shapes and size with different font size which made it inconvenient for analysing or for the prescribers as well as patients for reference.

Out of the total 168 PIs that were analyzed, 158 were from Indian companies and 10 from multinational companies.(Figure 1).Among them 134 (79.7%) were oral and 34 (20.3%) were injectable preparations. (Figure 2).

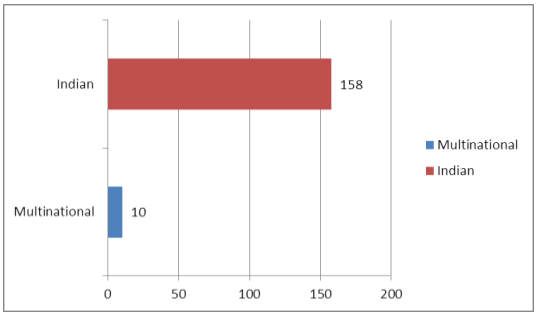

Figure 1

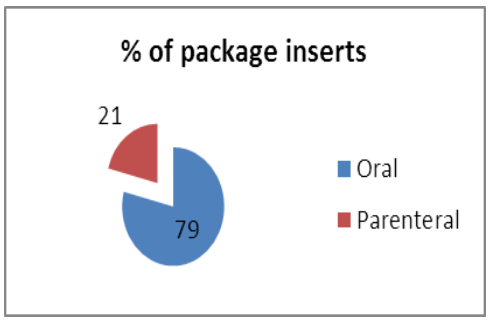

Figure 2

They were divided class wise as follows: 30 were for antimicrobial agents, 27 were for anti-diabetics,22 were for acid lowering agents and antacids as well as for anti-hypertensives, 21 were analgesics,18 were multivitamins, 15 were hypolipedemics,5 were iron chelators, 2 were vaccines,4 were anti snake venom sera and 2 was anti arrhythmic.(Figure 3).

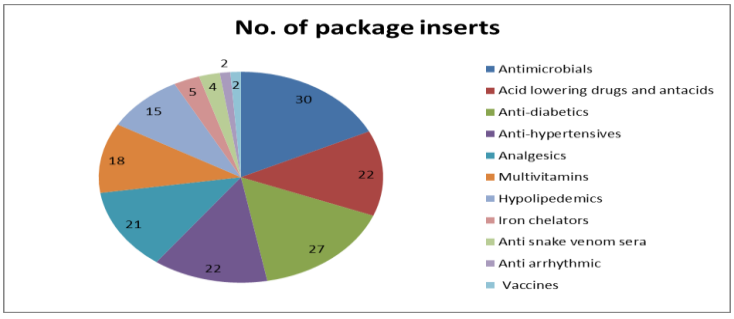

Figure 3

As per schedule D, it is necessary to mention both sec 6.2 and sec 6.3 in the package insert. But it was found that much importance was given to sec 6.2 as compared to sec 6.3 by the pharmaceutical companies. The information of sec 6.2 was nearly mentioned in all the inserts as in Table 1.

Table 1

No	Criteria	Present N (%)	Absent N (%)
1	Legibility	168 (100%)	-
2	Approved generic name of active ingredient	168 (100%)	-
3	Content of active ingredient per dosage form	168 (100%)	-
4	Generic names of other ingredients	158 (94.04%)	10 (5.95%)
5	Therapeutic indications	168 (100%)	-
6	Posology and method of administration	168 (100%)	-
7	Contraindications	168 (100%)	-
8	Special warnings and precautions	168 (100%)	-
9	Drug interactions	168 (100%)	-
10	Pregnancy and lactation	52 (30.95%)	116 (69.04%)
11	Pediatric and geriatric indications	48 (28.57%)	120 (71.42%)
12	Special conditions and contraindications	168 (100%)	-
13	Effect on ability to drive and use machines	30 (17.85%)	138 (82.14)
14	Undesirable effects	168 (100%)	-
15	Drug dose	168 (100%)	-
16	Antidote for over dosage	150 (89.28%)	18 (10.71%)

A wide discrepancy of data was noted in sec 6.3. (Table 2). The pharmaceutical information had several deficiencies. The list of excipients was mentioned in 92% inserts Shelf life is very significant for any drug. It was seen that shelf life was mentioned only in 26.1% inserts. However, shelf life after dilution and shelf life after first opening the container was given much less importance as compared to the shelf life as packed for sale. References to support the data were quted in only 2% package inserts.

Table 2

17	Pharmacokinetic information	88 (52.38%)	80 (47.61%)
18	Storage information, list of excipients	156 (92.85%)	12 (7.14%)
19	Instructions for use and handling	168 (100%)	-
20	Shelf life		
	i)Shelf life in the medical product as packed for sale	44 (26.1%)	124 (73.9%)
	ii)Shelf life after dilution or reconstitution according to direction	17 (10.11%)	151 (89.88%)
	iii) Shelf life after first opening the container	31(18.4%)	137 (81.54%)
21	Date on which information was last updated	10(11.90%)	74(88.09%)
22	Name and address of manufacturer/distributor	168 (100%)	-
23	Provision of full information on request should be highlighted	168 (100%)	-
24	Retail price of the drug	3 (3.57%)	81(96.42%)
25	References	2 (2.38%)	82(97.61%)

Out of 168 PIs, 118 (70.24%) belonged to Grade 'B' and remaining 50 (29.76%) to Grade 'A'. None of the PIs belonged to Grade 'C'.(Table 3)

Table 3

Score	Grade	Number of PIs	% of PIs
> 20	**A**	50	(29.76%)
10-20	**B**	118	(70.24%)
< 10	**C**	-	-

DISCUSSION

On analysing the package inserts, it was found that presentation of information was not uniform and it was difficult to locate and retrieve information easily due to lack of common layout and heading. Moreover, the package inserts were of different shapes and sizes with different font size which made it inconvenient for analysing or for the prescribers as well as the patients for

reference. The information presented in the PIs is necessary for both the prescribers and the patients. A study done in private practitioners concluded that the majority of them (72%) found package inserts useful or extremely useful. From patients point of view, PIs have an important impact on patient compliance and thus on the effectiveness of drug use.[6]

In contrast to the previous two studies, the clinical information represented in the package inserts which were evaluated in our study was relatively complete. Although there is an improvement in the quality and content of Indian package inserts over time, [7, 8] but still there are areas which remain unaddressed. It is important to realise that, apart from prescriber and pharmacist, patients are also end users of package insert. Currently in India, the structure and content of the information on the inserts is geared towards prescribers only. Given the fact that unauthorized over the counter drug dispensing is a prevalent practice in India, and that the patient education is still in infancy [9], there is an unambiguous need for package inserts to be more patient-friendly and specifically designed to avoid medication errors. This can be achieved by conducting regular surveys to model the package inserts for the population. There are many examples of such surveys done in developed countries with an aim to improve the package insert and make them user friendly for patients.[10]

India is a country with many languages and most people are not fluent, or even familiar with the English language. User testing of labels and package inserts are mandatory in many countries, but not in India. Yet, Schedule D pertaining to labelling, instructs manufacturers to print labels in English. This point had been taken note of in recent times and the Department of Chemicals of India had instructed manufacturers to print labels in Hindi as well.

However, this move met with significant hindrance as Hindi is not a predominant language in many parts of the country. For a manufacturer producing medicines for the entire Indian market, it is not possible to print labels in all relevant languages. A better means to improve comprehension could be to represent instructions pictorially. The manifest improvement of label-comprehension when dosage instructions are presented pictorially has been reported in the past.

Overall, there is a need to improve the format, content and language of the package inserts in India. Tighter monitoring of the inserts by regulatory bodies can help to enforce ideal labelling practices. Furthermore, the industry needs to revise its labelling methods. While there is a need to deliver necessary information accurately to the patient, it is also important from a logistical perspective to balance the information against over-sized leaflets that are clumsy to handle and daunting to the patient.[3]

The availability of a comprehensive database for the DCGI - approved package inserts in India, would be of much help for the proper and timely dissemination of healthcare information to the prescribers, as well as the patients.[1] From the above findings, it is suggested that the PIs must be optimized and tested by selected groups of experts prior to the approval of the drug. This will ensure the avoidance of the lack of information and will guide towards informed and better treatment outcomes. The supply of the PIs should be made mandatory in the package along with the drugs. The government should make strict rules to ensure that the pharmaceutical companies comply with the regulatory guidelines.

CONCLUSION

Thus, the current concept of Package insert, which is followed in India, is inadequate in serving its purpose of providing satisfactory prescribing guidance in an effective manner, to the prescribers or the patients. However, there is a huge scope for improvement in the same, as newer and better concepts have been successfully introduced in some of the developed nations. With the rising healthcare awareness in our society, and to minimize the incidence of medication error-related adverse events, an improvement in the current concept of Package inserts for dissemination of information, is a requirement that must be considered seriously.

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