Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

doi: 10.5455/2319-2003.ijbcp20130309

Research Article

Comparison of Indian package inserts in public and private sector: an urgent need for self regulation

Mohini S. Mahatme[a]*, Ganesh N. Dakhale[a], Sachin K. Hiware[a], Sumit S. Wankhede[a], Anoop M. Salve[a], Sachin R. Mahatme[b]

[a]Department of Pharmacology, Indira Gandhi Govt. Medical College, Nagpur–440018, India, [b]Consultant Radiologist, Nagpur, India

Received: 10 January 2013
Accepted: 27 January 2013

***Correspondence to:**
Dr. Mohini S. Mahatme,
Email: drmsm28@gmail.com

© 2013 Mahatme MS et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Package inserts are the authentic source of information for the new molecules in the market. Incomplete and incorrect product information may promote irrational prescribing and may have serious consequences. Hence, our aim was to analyse and compare the information supplied in the package insert according to the section 6.2 and section 6.3 of schedule D of Drugs and Cosmetic Act, 1940 in public (government) and private (non-government) sector.

Methods: Package inserts of allopathic drugs which were supplied by government from drug store of tertiary care centre and hospital and from pharmacies on request were collected. A total of 270 package inserts in English were collected that is 38 from government hospital and 232 from the pharmacies nearby the hospital. The package inserts were analysed for the presentation of completeness of the information as per section 6.2 and 6.3.

Results: The presentation of information on analysing 233 package inserts (28 government and 205 non government) 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 variable shape and size with different font size which made it inconvenient for analysing as well as for reference. Posology and method of administration was incomplete in 3% package insert in non- government cases whereas in government supply it was 7%. Use of drug in pregnancy and lactation was deficient in 11% and 14% packages inserts of non-government sources and government sources respectively. Instructions for use were lacking in 25% and 29% package inserts of government and non-government sources respectively.

Conclusions: The need of the hour is to further refine contents of the circulated package inserts to make them complete, reliable and up to date. This can be a step forward for ethical and effective dissemination of healthcare services in our growing society.

Keywords: Packet inserts, Therapeutic indications, Pharmaceutical information, India

INTRODUCTION

Package insert is an officially approved mandatory document inside the package with the intention to provide relevant, recent and unbiased information for rational drug use.[1] The information accompanying the drug is approved by the regulatory agencies.[2] Pharmaceutical companies promote information regarding marketed products through promotional literature, medical representatives, periodicals, continued medical education programme (CME) and package insets.[3] Package inserts are the authentic source of information for the new molecules in the market.[4] Accurate and reliable drug product information is very important for its safe and effective use. Incomplete and incorrect product information may promote irrational prescribing and may have serious consequences, including disability and death. Hence, this information must be constantly updated as and when any relevant preclinical and clinical data crop up.

Globally, there is considerable variation in the information included in the package insert or leaflet. Different countries have different regulatory bodies for package inserts. In United States, the regulatory authority

is Food and Drug Administration; in Europe it is European Medicines Agency whereas 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. This information should be according to the Sec 6.2 and 6.3 of Schedule D, 1940 Act.[5] Once the application is approved by the regularity authorities, the information is accompanied with the drug in the package.

The health care providers (physicians, pharmacists, nurses and community health workers) as well as the end users (patients) largely rely on the information provided by the manufacturers on the labelling of the products.[6] The package insert is primarily intended to guide the prescribers. The prescribing physician is the preferred information source for most of the patients. An effective communication may not always be practically possible between the prescribers and the patients. Information given verbally is likely to be either missed or forgotten. Moreover, considering the inadequate doctor/patient ratio in our country, the accessibility of trained prescribers for the entire population is very difficult. Therefore, it is now widely acknowledged that patients do require a certain amount of information in order to use their drugs optimally.[7] Package inserts have an important impact on the patient's compliance and thus on the effectiveness of drug use as it is seen by the patients only after receiving the medicine. If these are designed properly, i.e. by giving accurate and complete information about precautions, adverse effects, it may promote rational medication or prevent self-medication which is one of the main causes of the increasing ADRs incidence in our country. Recent studies have found that inserts are still missing key information regarding a drug′s safety and efficacy.[8] Presently, the package insert has become more of the legal formality rather than an effective tool for providing timely and accurate prescribing guidance.

Hence, keeping all this background in mind, we considered it worthwhile to analyse the completeness of information of package inserts according to the section (sec.) 6.2 and 6.3 of schedule D of Drug and Cosmetic Act, 1940 and to compare the package inserts supplied in public(government) and private(non government) sector.

METHODS

As per section 6.2 and 6.3 of schedule D, it is necessary that all package inserts should contain information pertaining to the different therapeutic indications and pharmaceutical information listed by the Government of India. If the information is not present, atleast a disclaimer statement regarding the lack of such information should be made by the company. Package inserts of allopathic drugs were collected on request from the drug store of government sector and from the pharmacies. Ayurvedic products were excluded from the study. A total of 270 package inserts in English were collected that is 38 from government hospital and 232 from the pharmacies nearby the hospital. As per sec 6.2, it is mandatory that the package inserts should be in English only. Hence, the inserts in regional language were excluded from the study. The duplicate leaflets (same drug, same formulation and same company) were also excluded. The package inserts were analysed for the presentation of completeness of the information as per sec 6.2 and 6.3. Each heading mentioned on sec 6.2 and 6.3 were checked followed by the scrutiny of the information included under the heading. If the heading was not present in the leaflet, the entire insert was checked for the relevant information to the concerned heading. However, if the information was present even elsewhere, it was included in the analysis.

The prescribing information should include the following details of sec 6.2 (therapeutic indications) i.e. posology and method of administration, contraindication , special warning and special precaution for use if any, interaction with other medicaments and other form of interaction, pregnancy and lactation if contraindicated, effect on ability to drive and use machines if contraindicated, undesirable/side effects, antidote for overdosing. Section 6.3 (pharmaceutical information) includes list of excipients, incompatibility, shelf life in the medical product as packaged for sale, shelf life after dilution or reconstitution according to dilution, shelf life after opening the container, special precaution for storage, nature and specification of the container, instruction for use/handling. The analysis of data was expressed as absolute number and percentage.

RESULTS

A total of 270 leaflets were collected during the study period, of these 37 package inserts were excluded from the study due to duplication. Hence, only 205 from pharmacies and 28 package inserts from government hospital were included for further analysis. The 233 package inserts included 93 oral, 91 injected and 49 miscellaneous items/topical preparations marketed by different pharmaceutical companies in India.

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 size with different font size which made it inconvenient for analysing or for the prescribers as well as patients for reference. 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. It was seen that in 22 package inserts collected from non- government sources, generic name was not written whereas, in package inserts

collected from government sources, generic name was not mentioned in 5 package inserts. Posology and method of administration was incomplete in 3% package insert in non- government cases whereas in government supply, it was 7%. Contraindications to the drug use, which forms a very important part for drug prescribing, was mentioned in 93% package inserts of non- government sources while 96% inserts of government sources contained the information. Interactions with other medicaments and other forms of interaction were mentioned only in 79% of the package inserts of non-government source and 82% of inserts of government source. It was found that much stress was given to the interactions with other medicaments. Drug food interaction was mentioned in hardly 35 inserts of the total 233 inserts. The information pertaining to other points of sec 6.2 are depicted in Table 1.

Table 1: Comparison of therapeutic indications as per section 6.2 in government and non government package inserts.

S. No	Contents	Government package inserts		Non government package inserts	
		Mentioned (percentage)	Not mentioned (percentage)	Mentioned (percentage)	Not mentioned (percentage)
1.	Indication	28 (100%)	0	205 (100%)	0
2.	Posology and Method of administration	26 (93%)	2 (7%)	199 (97%)	6 (3%)
3.	Contraindications	27 (96%)	1 (4%)	190 (93%)	15 (7%)
4.	Special precaution/ warnings for use, if any	28 (100%)	0	194 (95%)	11 (5%)
5.	Interactions with other medicaments and other forms of interaction	23 (82%)	5 (18%)	162 (79%)	43 (21%)
6.	Pregnancy/ lactation, if contra-indicated	24 (86%)	4 (14%)	182 (89%)	23 (11%)
7.	Effect on ability to drive and use machines, if contra-indicated	7 (25%)	21 (75%)	43 (21%)	162 (79%)
8.	Undesirable/side effects	27 (96%)	1 (4%)	190 (93%)	15 (7%)
9.	Antidote for overdosing	18 (64%)	10 (36%)	135 (66%)	70 (34%)

Table 2: Comparison of pharmaceutical indications as per section 6.3 in government and non government package inserts.

S. No	Contents	Government package inserts		Non government package inserts	
		Mentioned (percentage)	Not mentioned (percentage)	Mentioned (percentage)	Not mentioned (percentage)
1.	List of excipients	21 (75%)	7 (25%)	90 (44%)	115 (56%)
2.	Incompatibilities	14(50%)	14(50%)	77 (38%)	128 (62%)
3.	Shelf life in the medical product as packed for sale	10 (36%)	18 (64%)	59 (29%)	146 (71%)
4.	Shelf life after dilution or reconstitution according to direction	10 (36%)	18 (64%)	25 (12%)	180 (88%)
5.	Shelf life after first opening the container	11 (39%)	17 (61%)	44 (21%)	161 (79%)
6.	Special precaution for storage	27 (96%)	1 (4%)	171 (83%)	34 (17%)
7.	Nature and specification of the container	16 (57%)	12 (43%)	181 (88%)	24 (12%)
8.	Instructions for use	21(75%)	7 (25%)	145 (71%)	60 (29%)

Table 3: Comparison of other information in government and non government package inserts.

S. No	Contents	Government package inserts		Non government package inserts	
		Mentioned (percentage)	Not mentioned (percentage)	Mentioned (percentage)	Not mentioned (percentage)
1.	Clinical pharmacology	20 (71%)	8 (29%)	168 (82%)	37 (18%)
2.	Pharmacokinetics	14 (50%)	14 (50%)	147 (72%)	58 (28%)
3.	Information update date	8 (29%)	20 (71%)	36 (18%)	169 (82%)
4.	Pediatric use	24 (86%)	4 (14%)	141 (69%)	64 (31%)
5.	Geriatric use	25 (89%)	3 (11%)	161 (79%)	44 (21%)
6.	Clinical trial	6 (21%)	22 (79%)	53 (26%)	152 (74%)

Table 2 represents the pharmaceutical information. A wide discrepancy of data was noted in sec 6.3. The pharmaceutical information had several deficiencies. The list of excipients was mentioned in 75% inserts of government supply whereas it was not mentioned in 56% package inserts collected from non-government sources. Shelf life is very significant for any drug. It was seen that shelf life was mentioned only in 36% inserts of government supply and only in 29% inserts of non-government supply. 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. Nature and the specification of the container, which had grave pitfalls, were enlisted in 57% and 88% government and non government package inserts respectively.

We also analysed additional information supplied in the package inserts as in Table 3. Clinical pharmacology was mentioned in 71% package inserts of government supply and 82% package inserts of non-government supply. Pharmacokinetic data was there in 50% and 72% package inserts of government and non-government sources. The information was updated only in 29% and 18% package inserts of government and non-government sources. The data regarding adverse effects of the clinical trial was mentioned only in 6 and 53 package inserts of government and non-government supply.

DISCUSSION

To the best of our knowledge, this is the first study to analyse both the sections of therapeutic indications (6.2) and pharmaceutical information (6.3) simultaneously. After undergoing extensive literature search, we could not find even a single study which compared both the sections of Schedule D. Moreover, this is the only study to compare the packet inserts in public and private sector. Therefore, at present situation, it is not possible for us to compare our study with any other study for section 6.2 and 6.3 concurrently. On analysing the data, we found the information for the safe and effective use of drugs is missing as packet insert was not provided with some drugs. This was noticed more in the packages of the drugs supplied in the government institutions by the companies entitled to supply the drugs for the government as compared to the package inserts which were collected from outside pharmacies i.e. non government sources. As we have collected the package inserts for duration of six months i.e. March 2012 – August 2012, we could assemble only 28 package inserts of drugs supplied to the medical store in the government institution. This is due to lack of vigilance on the pharmaceutical companies for ensuring the supply of the package inserts in the packages.

The current concept of package inserts is inadequate in seeing its purpose of providing satisfactory prescribing guidance to the prescribers. The complexities in the format of the package inserts act as a barrier to the intended usage. The lack of uniformity in size, shape, font causes inconvenience to the prescribers as well as patients. When compared with the findings of sec 6.2 of the previous studies,[2,9] there was an overall improvement in the information. However, the deficiency of the information in section 6.2 and section 6.3 depicts that there is no strict vigil on the package inserts supplied from the pharmaceutical companies by the licensing authorities. This could be attributable to lack of any gold standard guidelines or rules by the administrative licensing authority in India, for the accuracy of package inserts. If a standard had been set by the authority, each and every part of schedule D would have gained equal importance, leading to the ideal package inserts.

The information presented in the package insert is necessary for both i.e. the prescribers and the patients. A study done in private practitioners observed that the majority (72%) found package inserts useful or extremely useful. Reason for consulting the package insert, in order of frequency were information on effects (64%), indications (33%) and mechanism of action (33%).[10] With rising healthcare awareness in our society, the incidence of medication error related adverse events are also increasing. Other important reason for increase in adverse effects in country like ours is self medication. The package insert is seen by the patient only after getting the medicine. Package inserts have an important impact on patients compliance and thus on the effectiveness of drug use. The traditional package insert followed in India,

needs a revision so that it can be used in a more effective manner.

The concept has to be modified such that it can serve as a better tool for the dissemination of information to the patients and the prescribers. To minimize medication related adverse events, an improvement in the current concept for dissemination of information must be considered seriously. To improve the readability and comprehensiveness of package inserts, they 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 the information and will give the best possible outcome to avoid safety risks. The supply of the package inserts should be made mandatory in the package along with the drugs. The government should make strict rules with the unique format of the package insert so that the discrepancies regarding the paper size, shape, font size are removed irrespective whether it is solid, liquids, cream and gels. A governing body should be formed to ensure the implementation of these rules.

Self regulation by the pharmaceutical companies can also be the part of the solution. The pharmaceutical companies should also abide by the rules and support the licensing authorities to ensure the effectiveness of the drug use. They should tout the completeness, validity and up gradation of information in their products package inserts.

CONCLUSION

Package inserts have an important impact on the patients compliance and thus on the effectiveness of drug use. However, the need of the hour is to further refine the contents of the circulated package inserts to make them complete, reliable and up to date. This can be a step forward for ethical and effective dissemination of healthcare services in our growing society.

Funding: None
Competing interests: None declared
Ethical approval: Not required

REFERENCES

1. Ved JK. Package Inserts in India: Need for a Revision. Int J Pharm Res Sci 2010;1:454-6.
2. Shivkar YM. Clinical information in drug package inserts in India. J Postgrad Med 2009;55:104-7.
3. Pujari P. Analysis of information provided in drug package inserts in India. Indian J Pharmacol 2011;43:S27.
4. Fuchs J, Hippius M, Schaefer M. Analysis of German package inserts. Int J Clin Pharmacol Ther 2006;44:8-13.
5. Govt. of India, Ministry of Health and Family Welfare. Drug and Cosmetics Rules 1940. P- 312. Available at http: //cdsco.nic.in/html/Drugs and CosmeticAct.pdf. Accessed 28 July 2012.
6. Amran S, Ahmed M, Shaheen SM, Morshed SN, Khandakar J, Rahman M, Rahman M, Hossain A. Short communication: a study on the packaging information of essential drug products used at Union and Thana health complex level in Bangladesh. Pak J Pharm Sci 2007;20:327-32.
7. Suleh A Bawazia, Hisham S Abou- Auda, Othman A Gubara, Khal III Al- Khamis, Mohammed JMS Al- Yamani. Public Attitude towards Drug Technical Package Inserts in Saudi Arabia. J Pharm Technol 2003;19:209-18.
8. Zaghi D, Maibach HI. Survey of safety and efficacy information in drug inserts for topical prescription medications. Am J Clin Dermatol 2007;8:43-6.
9. Lal A, Sethi A. Drug package inserts in India. Ann Pharmacother 1996;30:1041.
10. Joubert PH, Skene D. Attitudes of private medical practitioners towards package inserts and other drug information source. S Afr Med J 1984;66:306-7.

doi:10.5455/2319-2003.ijbcp20130309
Cite this article as: Mahatme MS, Dakhale GN, Hiware SK, Wankhede SS, Salve AM, Mahatme SR. Comparison of Indian package inserts in public and private sector: an urgent need for self regulation. Int J Basic Clin Pharmacol 2013;2:165-9.