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CRITICAL APPRAISAL OF DRUG PACKAGE INSERTS: A STUDY AMONG MEDICAL STUDENTS

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ABSTRACT

Background: Package inserts (PIs) are critical tools in drug labelling, offering evidence-based information to ensure the safe and effective use of medications. In India, the format and content of PIs are governed by the Drugs and Cosmetics Act (1940) and Rules (1945), specifically Schedule D, Sections 6.2 and 6.3. However, studies indicate inconsistencies in the completeness of PIs. Well-structured PIs also serve as practical learning tools for medical students. This study aimed to critically evaluate the clinical and pharmaceutical content of PIs marketed in India, using regulatory standards.
Methods: A cross-sectional study was conducted among 150 second-year medical students from a Government Medical College in Kerala, India. Each student assessed one PI using a standardized 34-item checklist based on regulatory guidelines and published literature. Each item was scored as present (1) or absent (0). Based on total scores, PIs were classified as Grade A (24–34), Grade B (13–23), or Grade C (0–12).
Results: Of the 150 PIs reviewed, only 62.67% used appropriate font size and 68% used proper font colour. Core content like generic name, dosage, and indications was present in all PIs. However, safety-related data such as ADR classification (45.33%), drug interactions (90.67%), and ADR reporting instructions (43.33%) were inconsistently reported. Among 40 injectable PIs, gaps were noted in incompatibility and storage data. Overall, 35 PIs were graded A, 53 as B, and 12 as C.
Conclusion: Significant variability in PI content highlights the need for improved standardization and regulatory oversight. Incorporating PI evaluation into medical training may enhance safe prescribing and drug literacy.

Keywords: Package Inserts, Regulatory Standards, Critical Evaluation, Medical Students.

INTRODUCTION

Drug labelling is an important aspect of pharmaceutical regulation and patient safety. It includes all printed information accompanying a medicine, such as the label, packaging, and the package insert (PI).[1] The PI is a key regulatory document that provides evidence-based information to facilitate the safe and effective use of medications. Also referred to as the prescription drug label or prescribing

information,[2,3] its content is based on current scientific data and is updated as new preclinical and clinical findings emerge.[4]

Regulatory requirements for PIs vary internationally. In India, the *Drugs and Cosmetics Act (1940)* and *Rules (1945)* govern PI content, particularly under Section 6 of Schedule D (II).[5,6] Section 6.2 mandates that PIs be written in English and include therapeutic indications, dosage, administration, contraindications, precautions, interactions, use in pregnancy and lactation, effects on machinery operation, adverse effects, and overdose management. Section 6.3 requires pharmaceutical details such as excipients, incompatibilities, shelf life, storage, container specifications, and usage instructions.[5,6]

Though primarily intended for registered medical practitioners, hospitals, and laboratories,[7] the law does not clearly indicate whether PIs are also meant for patients.[8] Nevertheless, their structured format makes them a reliable information source for healthcare providers.[9] In countries like India, with a doctor-to-patient ratio below the WHO-recommended 1:1000[10] and prevalent self-medication practices, accessible PIs are even more vital. High-quality PIs can reduce prescribing errors, which account for 29% to 56% of medical mistakes,[11] and help bridge communication gaps between providers and patients.[8,12]

PIs also serve as valuable educational tools for medical students, offering concise information on drug properties that align closely with the pharmacology curriculum. Access to standardized, real-world drug information enhances their clinical competence, supports rational prescribing, and fosters independent learning. Despite regulatory frameworks, prior studies suggest inconsistencies in the quality and completeness of PIs in India.[13-15] Against this backdrop, the present study was conducted to critically appraise the clinical and pharmaceutical content of PIs available in the Indian market, based on regulatory guidelines, with evaluations carried out by medical students.

MATERIALS AND METHODS

This was a cross-sectional, questionnaire-based study conducted among 150 second-year medical students from a Government Medical College in Kerala, India. All participants had successfully completed their pharmacology examinations at the time of enrolment, ensuring a foundational understanding of drug-related information. The study was conducted over a period of two months, from August to September 2020, following approval from the Institutional Review Board (IRB) and the Institutional Ethics Committee. The objectives and procedures of the study were clearly explained to all participants, and written informed consent was obtained in accordance with ethical research standards.

Study Procedure

The research was conducted during Pharmacology Practical Sessions held over three consecutive days. During these sessions, the Principal Investigator delivered an educational lecture on the importance of Package Inserts (PIs) and guided students on how to critically evaluate their contents. After the lecture, each participant received one PI from a pool of inserts collected from local pharmacies. A total of 150 PIs, all printed in English, were included. These encompassed a range of dosage forms, including 110 oral and 40 injectable preparations, across various therapeutic categories, such as antidiabetics, antibiotics, antihypertensives, antimalarials, hormonal agents, antihistamines, antiemetics, and analgesics. The PIs belong to various Indian pharmaceutical companies.

Exclusion Criteria for PIs Included

- Inserts from Ayurvedic or traditional medicine products
- Duplicate inserts from the same brand
- Inserts printed solely in regional languages

However, PIs printed in both English and a regional Indian language were accepted for inclusion.

Evaluation and Scoring Criteria

Prior to distribution of PIs, all participants were briefed on the objectives and methodology of the critical appraisal exercise. All 150 students who provided informed consent were included in the study. Each student was then instructed to critically evaluate a single PI using a standardized proforma, which was formulated in accordance with the Drugs and Cosmetics Rules, 1945 (Schedule D, Sections 6.2 and 6.3), and supplemented with parameters from previously published literature. Using this comprehensive 34-item checklist, participants were required to assess both the completeness and clarity of the information provided in the PI. In cases where a specific heading was absent, the insert was carefully reviewed to determine whether the relevant information was included under a different section or heading.

The following parameters were considered during the detailed assessment of each PI:

- Presence of mandatory headings as per Section 6.2, including: Therapeutic indications, posology and method of administration, contraindications, special warnings and precautions, drug interactions, use during pregnancy and lactation, undesirable effects, and antidote for overdose
- Inclusion of pharmaceutical data required under Section 6.3, such as:List of excipients, known incompatibilities, shelf life, special storage conditions, container description, and instructions for use and handling
- Evaluation of the uniformity, accuracy, and clarity of information presented under each heading
- Legibility of the PI, assessed in terms of font size and font colour

Upon completion of the appraisal, the responses from these students were reviewed for completeness and included in the final statistical analysis. Grading of PIs was also carried out. For that each checklist item was scored in a binary format: a score of '1' was awarded if the required information was present, and '0' if it was absent. The maximum possible score for a complete PI was 34. Based on the total score, PIs were classified into three quality grades:

- Grade A (Good Quality): Total score between 24 and 34
- Grade B (Moderate Quality): Total score between 13 and 23
- Grade C (Poor Quality): Total score between 0 and 12

This grading system enabled a standardized assessment of the completeness and quality of PI content and facilitated the identification of deficiencies and variations in regulatory compliance.

RESULTS

Following the critical evaluation of 150 package inserts (PIs) by the participants, it was observed that only 94 (62.67%) of the PIs employed an appropriate font size, and 102 (68%) used a suitable font colour, indicating that a considerable number failed to meet basic standards for visual accessibility. Furthermore, the lack of a standardized format and inconsistent ordering of headings impeded the convenient retrieval of specific information, adding to user difficulty. The analysis revealed that certain core elements were consistently included in all PIs. Specifically, the generic name of the active ingredients, composition of ingredients, dosage form, posology and method of administration, and therapeutic indications were present in all 150 (100%) inserts.

Moreover, critical safety-related information such as contraindications were present in 148 (98.67%), undesirable effects / ADRs were included in 143 (95.33%), special warnings and precautions were found in 140 (93.33%), use of that particular during pregnancy and lactation was documented in 143 (95.33%) and name and address of the manufacturer were stated in 147 (98%). However, some essential components were less consistently reported.

For instance, drug interactions which are crucial for preventing adverse drug events were mentioned only in 136 (90.67%) of PIs. Information on retail price was mentioned in 131 (87.33%), pharmacokinetic and pharmacodynamic properties were detailed in 122 (81.33%), overdosage management was specified in 127 (84.67%), paediatric and geriatric indications were included in 125 (83.33%), provision for obtaining full information on request was highlighted in 121 (80.67%) and storage information was present in 112 (74.67%).

Several vital safety parameters were poorly represented. These include timing of drug intake in relation to meals was found in 98 (65.33%),effect on ability to drive or use machines was mentioned

in 76 (50.67%), ADR classification based on organ/system/class was present in 68 (45.33%), measures to be taken in case of ADR were specified in 68 (45.33%), instructions for reporting suspected ADRs were found in 65 (43.33%) and date of last update was mentioned in only 61 (40.67%).

Other sparsely documented elements included: contact details for the Pharmacovigilance Programme of India (PvPI) specified only in 56 (37.33%), qualitative frequency statements (e.g., common, rare) given only in 56 (37.33%) and guidance on missed doses specified only in 56 (37.33%).

Among the 150 PIs evaluated, 40 belong to injectable drug formulations. Within this subgroup, important data such as shelf life were mentioned in 37 (92.50%), instructions for use and handling described in 35 (87.50%), list of excipients given in 33 (82.50%), description of the container found in 31 (77.50%), incompatibilities mentioned in 29 (72.50%) and special storage precautions were found in 27 (67.50%). These findings highlight important gaps, particularly in the documentation necessary for the safe administration and storage of injectable medications. Table 1 and 2, below summarizes the percentage of PIs in which each type of information was present.

Sl. No.	Headings in the Package Inserts	Present	Percentage	Absent	Percentage
1	Legibility- Appropriate font size	94	62.67%	56	37.33%
2	Legibility- Appropriate font colour	102	68.00%	48	32.00%
3	Approved generic name of active ingredients	150	100.00%	0	0.00%
4	Composition of ingredients	150	100.00%	0	0.00%
5	Dosage form	150	100.00%	0	0.00%
6	Posology and methods of administration	150	100.00%	0	0.00%
7	Therapeutic indications	150	100.00%	0	0.00%
8	Contraindications	148	98.67%	2	1.33%
9	Special warnings and precautions	140	93.33%	10	6.67%
10	Maximum dose of drug is mentioned	116	77.33%	34	22.67%
11	Drug interactions	136	90.67%	14	9.33%
12	Pregnancy and lactation	143	95.33%	7	4.67%
13	Pediatric and geriatric indications	125	83.33%	25	16.67%
14	Effect on ability to drive and use machines	76	50.67%	74	49.33%
15	Undesirable effects	143	95.33%	7	4.67%
16	Pharmacological Properties- Pharmacokinetic and Pharmacodynamic properties	122	81.33%	28	18.67%
17	Special conditions and contraindications	124	82.67%	26	17.33%
18	Over dosage	127	84.67%	23	15.33%
19	Storage information	112	74.67%	38	25.33%
20	Instruction for use and handling	62	41.33%	88	58.67%
22	Date on which information was last updated	61	40.67%	89	59.33%
23	Name and address of manufacturer/distributor	147	98.00%	3	2.00%
24	Provision of full information on request should be highlighted	121	80.67%	29	19.33%
25	Retail price of the drug	131	87.33%	19	12.67%
26	References	56	37.33%	94	62.67%
27	Provides information on when to take the drug-(before/after/with meals)	98	65.33%	52	34.67%
28	Provides information on what to do if doses are missed	56	37.33%	94	62.67%
29	ADR classified based on organ system classes	68	45.33%	82	54.67%

30	Provides qualitative statements on frequency of side effects(rare/common)	56	37.33%	94	62.67%
31	Verbal frequency terms are explained in the form of natural frequencies (eg very common-more than 1 in 10 patients)	56	37.33%	94	62.67%
32	Describe suitable measures in case of ADR	68	45.33%	82	54.67%
33	Details on Reporting suspected ADR	65	43.33%	85	56.67%
34	Contact number of PvPI is given	56	37.33%	94	62.67%

Table 1: Presence of Key Information in Evaluated Package Inserts (n = 150)

	Headings in the Package Inserts	**Present**	**Percentage**
1	List of excipients	33	82.50%
2	Incompatabilities	29	72.50%
3	Shelf life	37	92.50%
4	Special precaution for storage	27	67.50%
5	Nature and contents of container	31	77.50%
6	Instruction for use and handling	35	87.50%

Table 2: Subgroup: Injectable Formulations (n = 40)

In addition to the qualitative evaluation, each Package Insert (PI) was subjected to a quantitative scoring and grading process based on a standardized checklist. Each item on the checklist was evaluated using a binary scoring system: a score of '1' was assigned if the required information was present, and '0' if it was absent. The maximum attainable score for a complete PI was 34. Based on the total score, PIs were classified into three quality grades to facilitate interpretation and comparison. Of the 150 PIs evaluated, 36.66% were classified as Grade A (high quality), 48.66% as Grade B (moderate quality), and 14.66% as Grade C (poor quality). This grading system provided a standardized assessment of the completeness and quality of PI content and helped identify deficiencies and inconsistencies in adherence to regulatory standards.[15]

Grade	**Score**	**Number**
Grade A	Score (24-34)	55 (36.66%)
Grade B	Score (13-33)	73 (48.66%)
Grade C	Score (0-12)	22 (14.66%)

Table 3: Scoring of Package Inserts (n = 150)

DISCUSSION

The present study critically evaluated the content and presentation of 150 package inserts (PIs) from the Indian pharmaceutical market using a 34-item structured checklist, focusing on readability, completeness of information, and regulatory compliance. The findings indicate that while core clinical information was generally well-represented, several patient-relevant and safety-related elements were frequently missing.

Essential information such as the generic name, composition, dosage form, posology, and therapeutic indications was present in 100% of the PIs, aligning with findings from Indian studies by Shivkar et al. (2009) and Barkondaj et al. (2020).[15,16] Similarly, contraindications (98.67%) and warnings and precautions (93.33%) were widely included, reflecting adherence to regulatory requirements for clinical content.

However, only 62.67% and 68% of PIs adhered to readability standards such as appropriate font size and colour, respectively. These findings mirror earlier observations by Shivkar et al.[15] Dickinson et al.[17] and Momin et al.[18] who highlighted poor formatting and the negative impact of small fonts on comprehension.

Information related to special populations was suboptimal, such as data on drug use in paediatric and geriatric populations appeared in only 83.33% of PIs, and guidance for hepatic or renal impairment in 82.67%. Shivkar et al. also noted similar gaps in PIs, which may compromise rational prescribing in vulnerable groups.[15]

Pharmacokinetic and pharmacodynamic data were included in 81.33% of PIs, overdosage management in 84.67%, and storage instructions in 84.00%, all of which are crucial for clinical safety. Comparable deficiencies have been reported by Ganguly et al.[19]

Several safety and usability parameters were inadequately addressed: only 50.67% included warnings about operating machinery or driving, 41.33% offered instructions for use and handling, and only 40.67% specified the date of the last update. Just 37.33% cited references to support the clinical content. These omissions align with findings from Shivkar et al.[15] and Ganguly et al.[19] raising concerns about accuracy and relevance.

Patient-oriented content was also lacking: only 37.33% addressed actions for missed doses, 65.33% guided food intake timing, and 37.33% used natural frequency descriptors for side effects. Thakkar et al.[20] similarly reported poor inclusion of patient-friendly information in Indian PIs.

Adverse Drug Reaction (ADR) communication was particularly deficient. Only 45.33% included ADR classification, 43.33% provided reporting instructions, and just 37.33% mentioned contact details for the Pharmacovigilance Programme of India (PvPI). Thakkar et al.[20] and Ganguly et al.[19] noted similar inadequacies, highlighting the need for improved pharmacovigilance content.

Formatting inconsistencies were another significant issue. Variations in the organization of headings and sequence of information hinder efficient use by healthcare professionals. Shivkar et al.[15] and Ganguly et al.[19] identified such structural inconsistencies as barriers to usability. Adopting international formatting standards, such as those used by the European Medicines Agency (EMA) or US FDA, could enhance readability and reliability.

While previous studies have reported that complex medical language in PIs impedes patient understanding,[15,20] this was not a limitation in our study, as the assessment was performed by medical students. Nevertheless, these findings highlight the need for dual-format PIs-one for healthcare professionals and another simplified version for patients.

In summary, while the inclusion of essential clinical content is encouraging, the overall effectiveness of Indian PIs is compromised by inadequate readability, patient-centeredness, and omission of key safety information. These concerns echo those raised in previous studies by Shivkar et al.[15] Thakkar et al.[20] and Ganguly et al.[19] To address this gap, regulatory authorities must enforce standardized, comprehensive, and patient-friendly guidelines for PI design. Aligning Indian PIs with global best practices could significantly enhance their utility in ensuring safe and rational drug use.

Limitations

This study has a few limitations that should be considered when interpreting the results. First, the analysis was based on a sample of 150 package inserts (PIs) obtained from a specific region, which may not fully represent the quality of all PIs marketed across India. Second, although a structured checklist was used to maintain uniformity, certain elements such as legibility and patient-centeredness involved subjective evaluation, potentially introducing variability in interpretation. Third, the study provides a cross-sectional assessment of PIs at a single point in time and does not reflect any updates or improvements made subsequently by manufacturers.

CONCLUSION

The present study reveals significant gaps in the content and presentation of drug package inserts (PIs) marketed in India. While essential pharmacological information such as composition, dosage, and therapeutic indications were consistently included, critical aspects related to patient safety, readability, and regulatory compliance were often missing or inadequately addressed. Key deficiencies included poor legibility, absence of patient-oriented guidance (e.g., missed doses, food interactions), lack of adverse drug reaction (ADR) reporting information, and inconsistent formatting. Furthermore, the limited inclusion of update dates and clinical references raises concerns about the accuracy and

reliability of the data presented. These findings underscore the need for uniform formatting standards, improved patient-focused content, and stricter regulatory enforcement to enhance the utility of PIs as effective tools for both healthcare providers and patients. Aligning PI design with global best practices could significantly contribute to safer and more informed drug use in India.

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Ethical policy and Institutional Review board statement
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