IJBPAS, October, 2024, 13(10): 4838-4848

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

COMPARATIVE STUDY ON PRIMARY LABEL, PRIMARY CARTON LABEL AND PATIENT INFORMATION LEAFLET OF DICLOFENAC INJECTION

PATEL J*, THAKKER D, MEHTA J

Department of Pharmaceutics, Parul Institute of Pharmacy and Research, Faculty of Pharmacy, Parul University, At. Po Limda, Ta. Waghodia- 391760, Dist. Vadodara, Gujarat, India

***Corresponding Author: Dr. Janki Patel: E Mail: janki0410pharma@gmail.com**

Received 24th July 2023; Revised 25th Sept. 2023; Accepted 17th Dec. 2023; Available online 1st Oct. 2024

https://doi.org/10.31032/IJBPAS/2024/13.10.8352

ABSTRACT

This project's primary goal was to study the primary labels (PL) and primary cartons labels and patient information leaflets (PIL) for their suitability, harmonisation, and compliance with legal and regulatory standards. In the study, the PL, primary carton label, and PIL of innovator and generic products were evaluated side by side. For this study, three distinct marketed brands of diclofenac injection IP—the innovator product, classified as brand A, and two generic versions, coded as brands B and C—were taken into consideration. The purpose of the survey study, which was question-based, was to determine if nurses were aware of labelling problems. The study found that the PL, primary carton label, and PIL of the innovator product were devoid of negative, significant, and minor findings. However, it was discovered that all three types of observations were present in generic brands' PL, primary carton labels, and PIL. Nursing personnel were unaware of the mistakes detected in the labels and believed the information to be accurate because of their normal workload and the hectic hospital ward activities. It's necessary to assure uniform and standard text matter content across PL, primary carton labels and PIL, thus, avoiding misleading information to healthcare professionals and patients.

Keywords: Patient information leaflet, Primary label, Primary carton, Text matter, Harmonization, Diclofenac injection IP

INTRODUCTION

In pharmaceutical industry product is acceptably formulated only when it is properly packaged and labeled. It serves as a link between medicinal practitioner, pharmacist and patients. The labels on pharmaceutical products provide brief instructions that need to be followed by patient during his course on particular medication. Label not only serves as identity of the product but it also helps to prevent medication errors that could have occurred during administration of particular medicine.

Label and labeling [1]

Package labelling is defined as any text, graphics, or other materials that are printed on the product, its labels, or any other connected materials. Labeling is concise information about drug's quality, efficacy and safety. Product quality includes chemical composition of drug, strength, its physical state in which it is supplied and the rules for its storage and handling. Efficacy includes its indications, therapeutic effects and dosing instructions. Safety refers to side effects, toxicity, contraindications, specific drug, food, chemical, or disease interaction with the medication.

Guidelines for labeling pharmaceutical products: [2]

Food and drug administration serve one of the major responsibilities of governing the labelling requirements for pharmaceutical and healthcare products. The correct labeling of pharmaceutical product is essential for consumer safety.

- The label applied on the pharmaceutical product should be readable in different environmental conditions through its transport, distribution, storage and during its usage by patient. It is the responsibility of the label manufacturer to make sure that the label print is neat and understandable while the product manufacturers are responsible for complying the content of the product with the label.
- In regards with displaying the product information on the label, different pharmaceutical product has their own different requirements, information and claims that has to be stated on the label. Several important things included are:

  I. Official product name
  II. Active and inactive ingredients
  III. Drug Facts table
  IV. Purpose and use
  V. Warnings
  VI. Directions
  VII. Allergic reactions

- Materials which chose for labeling should be approved and regulated. The adhesive, coating and inks should be "low migration" meaning lowest chances of transfer of substance to drug or device.
- Labels should be inspected and checked for information is consistent and accurate.

Major Components of Label: [3]

The information conveyed by the manufacturer to the person who handles the product includes both healthcare professionals and patients. It can be in the form of following: -

- Primary label- The label upon the container that is in the direct container of the product.
- Secondary label- The label on the outer pack that holds the container of product.
- Product Information Leaflet/ Package Inserts (PI) - A leaflet accompanied with medicinal product that contains specific information for the healthcare professionals.
- Patient Information Leaflet (PIL) – a leaflet accompanied with medicinal product that contains specific information in simple or lay language for the patient.
- Summary of Product Characteristics (SmPC) – A document providing complete information on product characteristics for marketing and aimed at healthcare professionals.
- Dispensing label – It is a label that gives specific information to patient that is attached to package during the time of dispensing. E.g. Pharmacist attaches the label of dose administration frequency during the time of dispensing.
- Cautionary labels – It gives special instruction or advise to the patient while using the medicinal product.

Label on Parenteral Preparation: [4], [5]

- The strength and the total volumeare the primary requirement display on principal display panel for single and multiple dose injectable drug products.
- The dry solid drugs that are to be reconstituted is expressed in terms of total strength or percentage.
- The label should include *Added Substances, Excipients and Ingredients* along with their amount and proportions.

- The label should indicate the reason for addition of particular substance (e.g. for pH adjustment or to achieve isotonicity)
- The similar generic drugs name may be mistaken. Hence the difference should be highlighted.
- The medicine name printed horizontally along the length of ampoule rather than vertically to prevent confusions in similar names.

Drug information-Diclofenac:

Diclofenac is the phenylacetic acid derivative with molecular formula: $C_{14}H_{10}Cl_2NO_2Na$ and Non-Steroidal Anti-Inflammatory Drug (NSAID). Diclofenac inhibits cox-1 and cox-2, the enzyme that is responsible for production of prostaglandin. Prostaglandin molecule has its activity in pain and inflammation and its inhibition is the primary mechanism of diclofenac. Diclofenac is frequently used as first line therapy for acute and chronic pain and inflammation from variety of causes **[6]**.

Diclofenac sodium injection is clear colorless sterile solution for parenteral use. It is usually in its salt form for pH adjustment and better absorption.

Objective:

- To compare the Primary label, Patient Information Leaflet and Secondary label of three market formulations of Diclofenac sodium injection.
- To carry out survey of hospital staff nurses regarding their usage of pharmaceutical product in hospitals while treating patients.
- To find out printing errors (if any) on the product labels.
- To recommend suggestion for appropriate understanding of label to prevent any medication mishaps.

Materials:

The three selected preparations (A, B and C), magnifying glass, android camera, standard references, and PL, PIL and carton labels of all the three brands. A carefully crafted survey made for nursing staff for assessing their views on product labels.

Method: [6, 7]

- The three marketed brands of Diclofenac Sodium Injection IP were arbitrarily selected and bought for this study.
- To protect the identity of the maker, these brands were classified A, B, and C. Brand A was from Innovator Company and it was chosen as the baseline product for the comparison study. The brand B and C are well established market formulation of generic manufacturer.

- Using magnifying glass PIL, PL and carton label was checked since PL had small font size and hence was not visible clearly with naked eyes.
- All the labels were carefully reviewed and studied for the existence of pertinent material, the accuracy of the information, and any typos (if any).
- An android camera was used to record the observations for later use as proof.

Survey:

The nursing staff is the one who directly deals with the patient admitted in the hospital. Hence they daily come across usage and handling of different medication and its method to use. Therefore, it is necessary for them to take up safe measures and prevent any medication mishaps or serious complications that may arise due to any medication errors. Hence it is their duty to read and understand all the information conveyed on labels of the medication product and follow them accordingly. It is also their duty to communicate and report the error or mistakes (if any) found on the label with higher authority healthcare professionals.

Among the nursing staff, a survey was undertaken to ascertain their opinions on PL, PIL and carton labels. The questionnaire was circulated to 20 nurses and the objective of the study was explained to them. Their responses were collected and compiled and later analyzed.

RESULT AND DISCUSSION:

The critical review study revealed the following observations:

Storage Conditions Mentioned on the Primary Label and Carton: -

The storage requirement for formulation varied in brand C as compared to other 2 brands. It is outlined below.

Brand A: Store below 30°. Do not refrigerate. Protect from Light.

Brand B: Store below 30°. Protect from light. DO NOT FREEZE.

Brand C: Store at temperature not exceeding 30°.

The instruction to protect the product from light was not mentioned in brand C.

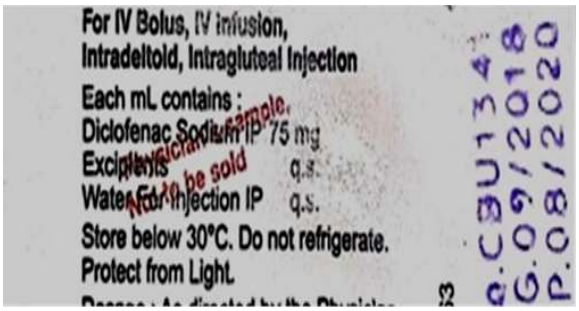


Figure 1: Storage conditions on Brand A

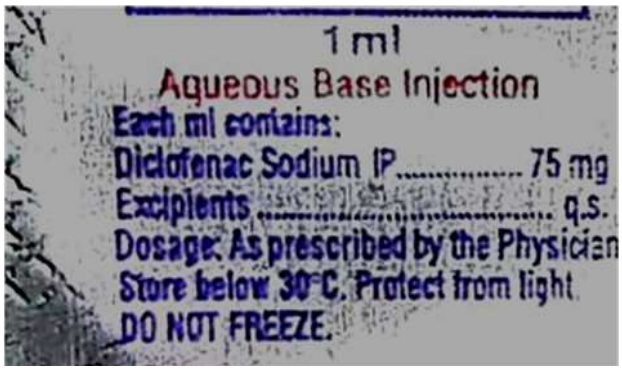


Figure 2: Storage conditions on Brand B

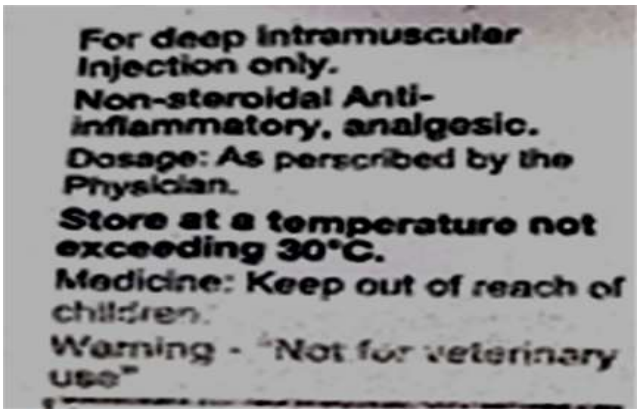


Figure 3: Storage conditions on Brand C

Observation Regarding Warning Label:

The SCHEDULE H DRUG warning label on Brand A product was not printed in red contrast background while Brand B and Brand C warning label was printed on red contrast background. It could be seen from the given **Figures 4-6**.

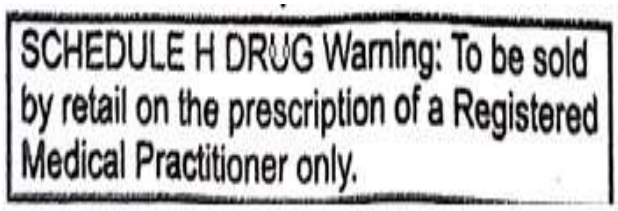


Figure 4: Warning label on Brand A

Figure 5: Warning label on Brand B

Figure 6: Warning label on Brand C

Observation Regarding Print Visibility and Clarity: -

The Brand B has print on the label which is partially faded and the essential information is improperly visible.

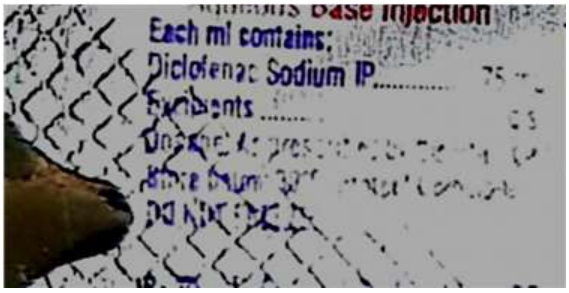


Figure 7: Brand B showing faded print information

Observation Regarding Presence of Precaution Advise: -

Brand A does not show any precaution advice related to usage before administration. This advisory precaution is not even found on PIL. Brand B shows precaution advice "Do not use if solution is not clear or has suspended matter."

Brand C shows precaution advice "Do not use if solution is not clear or has suspended matter."

It can be observed from below given **Figures 8-11**.

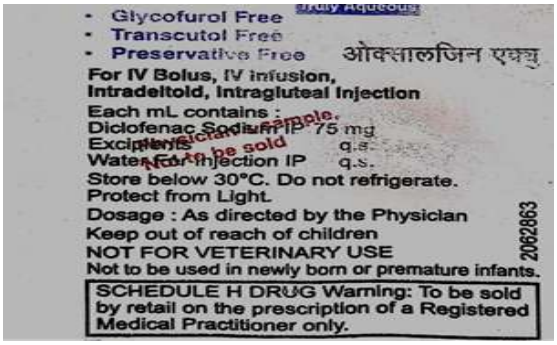


Figure 8: Secondary label of Brand A with missing precaution advisory label

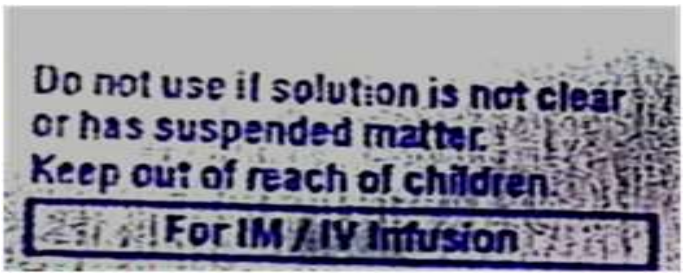


Figure 9: Secondary label of Brand B showing precaution advisory label

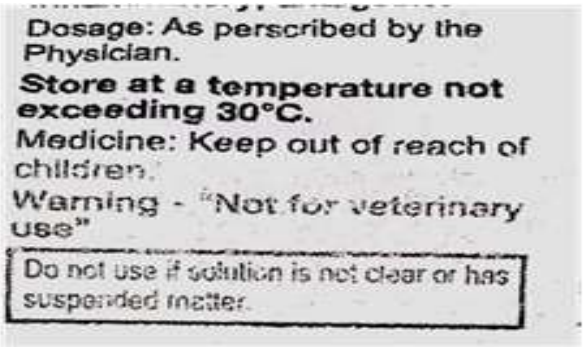
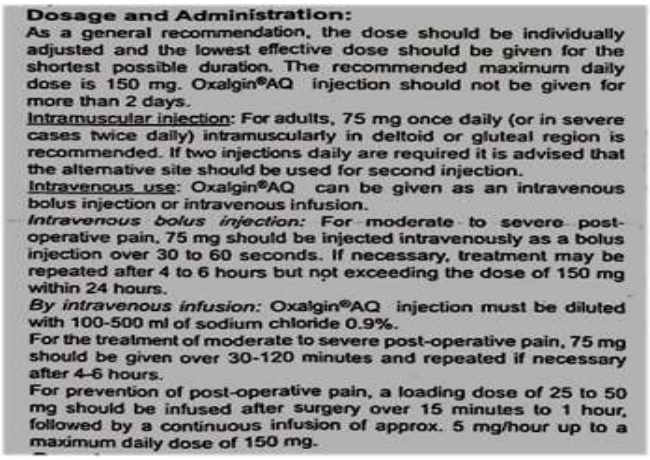


Figure 10: Secondary label of Brand C showing precaution advisory label



Dosage and Administration:

As a general recommendation, the dose should be individually adjusted and the lowest effective dose should be given for the shortest possible duration. The recommended maximum daily dose is 150 mg. Oxalgin®AQ injection should not be given for more than 2 days.

Intramuscular injection: For adults, 75 mg once daily (or in severe cases twice daily) intramuscularly in deltoid or gluteal region is recommended. If two injections daily are required it is advised that the alternative site should be used for second injection.

Intravenous use: Oxalgin®AQ can be given as an intravenous bolus injection or intravenous infusion.

Intravenous bolus injection: For moderate to severe post-operative pain, 75 mg should be injected intravenously as a bolus injection over 30 to 60 seconds. If necessary, treatment may be repeated after 4 to 6 hours but not exceeding the dose of 150 mg within 24 hours.

By intravenous infusion: Oxalgin®AQ injection must be diluted with 100-500 ml of sodium chloride 0.9%.

For the treatment of moderate to severe post-operative pain, 75 mg should be given over 30-120 minutes and repeated if necessary after 4-6 hours.

For prevention of post-operative pain, a loading dose of 25 to 50 mg should be infused after surgery over 15 minutes to 1 hour, followed by a continuous infusion of approx. 5 mg/hour up to a maximum daily dose of 150 mg.

Figure 11: PIL of Brand A with missing information on precaution advisory regarding administration before usage

Nursing staff's view on PL and PIL: -

Table 1 shows the Demographic characteristics of Participants. According to the nursing staff in the hospital, it was found that 80% of nursing staff read the basic information like dose, route of administration, contraindications, and side effects and checked the medicine name on PL and PIL. However from the study it was found that they often neglect the storage instructions. Though it was also found that 20% of nurses doesn't read any information on labels and leaflets. This includes nurses who are least experienced in the staff.

Table 1: Demographic characteristics of Participants

Table 1 : Demographic characteristics of Participants		
Demographic factors	**Number of participants**	**Percentage**
Sex		
Male	**2**	**25%**
Female	**6**	**75%**
Age wise distribution		
20-25	**7**	**87%**
26-30	**1**	**13**
Experience wise distribution (years)		
0-3	**7**	**87%**
3-6	**1**	**13%**

DISCUSSION

The labels on the pharmaceutical product are the essential guide for all healthcare professional as well as patients. Therefore it is necessary that the labels are free from any kind of typographical as well as medication errors. Such errors can cause misinterpretation of any information that can eventually lead to minor or major mishaps.

From the critical study of comparison between PL and PIL of different brands of Diclofenac sodium injection various discrepancies were found.

- The storage information was found to be incomplete in case of Brand C. It lacked information regarding protection from light which was mentioned in other 2 brands.
- The Warning label for SCHEDULE H DRUG which should be generally highlighted in red contrast background to catch the attention of individual was not found in case of Brand A. It may lead to selling of drug without prescription if the warning label in not read.
- The label on Brand B showed faded information which may lead to misinterpretation and misunderstandings. This would have occurred due to improper printing of low quality ink used for printing.
- The precaution advice regarding usage before administration, “Do not use if solution is unclear or has suspended matter.” was not found in Brand A.

The same information was missing in PIL of Brand A too, while the other 2 brands showed this information.

- The font size in case of Brand B was found to be too small to be readable with naked eyes. It may lead to misinterpretations.
- Other useful information present on all the 3 brands were appropriate and complied with the standard information.

However such minor errors could be prevented if the quality control check is carried out perfectly. Though the errors does not lead to any negative impact for healthcare professional since they have knowledge regarding the matter. But in case of usage of medication by less experienced personnel in healthcare there are probability for misinterpretations. Hence it is better to prevent such errors on labels. It should be a sole responsibility of healthcare professional to check the labels and report the faults.

SUMMARY:

Several Diclofenac sodium injections are available in market form different manufacturers. The formulation is available as branded products as well as generic ones. The label on the product may vary from different formulations. However, the information on PL and PIL should be complied with Food and Drug Administration and Indian Pharmacopoeia. The information on labels should be appropriate, legible and free from errors or mistakes. The Critical and Comparative study along with survey on PL and PIL has revealed little discrepancies in different brands which should be reported and prevented to avoid any medication mishaps.

CONCLUSION:

This study's findings that there is further need to check and review labels in case of all the brands under study and rectified for faults found on it. Firstly, it is the role of manufacturer to supply proper caliber of PL and PIL. The quality control check of the label information should be carried out with utmost care. The improper and incomplete information should not be neglected during sampling, reviewing and approving these labels. The necessary information like warning labels, advisory information, contraindications and drug interactions should be highlighted so that it would grab the direct attention of an individual who handles the product. The font size on the labels should be comparatively larger for easy readability. In case of SVPs (Small Volume Parenteral) like ampoules and vials the text printed should be horizontal rather than vertical so majority of information can be included on the label. The dark contrast background should be must for

warning advisory label. The ink used in printing labels should be rechecked for its quality. It should not get faded away or spread on the label. It should retain on the label during storage conditions and entire shelf life of the product. The Quality Control staff should be provided with effective training and evaluation of samples. This can be helpful to prevent the release of faulty labels in the market. From the survey of nursing staff, it was also found that due to hectic workload of nurses, they often avoid reading information on labels. Since it is the responsibility of healthcare staff to prevent any medication mishaps due to misinterpretations on label information, it is necessary to understand information and report faults (if any) to prevent any causalities. The sole responsibility here lies in the hands of Quality Control department to approve labels only which contain appropriate, legible and complied information and free from typographical errors, medication errors as well as print-related errors.

REFERENCES:

[1] U. K. Jain, D. C. Goupale and S. Nayak, Pharmaceutical Packaging Technology, Hyderabad: PharmaMed Press.

[2] "Custom Label Blog; Guidelines for labeling pharmaceutical and healthcare products," consolidated label company, [Online]. Available: https://consolidatedlabel.com/label-articles/guidelines-labeling-pharmaceutical-healthcare-products/.

[3] N. M. R. Authority, *Guidelines on Labeling and Information Leaflets of Medicines,* Sri Lanka, 2019.

[4] *United State Pharmacopoeia.*

[5] H. P. R. Authority, *Guide to Labels and Leaflets of Human Medicines.*

[6] Tippavajhala VK, Kumar L, Sathyanarayana MB, Thunga G, Chandran VP, Khan S, Kulyadi GP. A critical and comparative study on patient information leaflet, primary label and primary carton of a carbapenem dry powder injectable. 2019 Jan 1; 53(1):178-85.

[7] Indian Pharmacopoeia, 2018.