Elements of Prescription Drug Labels

A brief overview of prescription drug labeling for patients and providers.

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SINCE 2006, the U.S. Food and Drug Administration (FDA) has mandated both content and format of full prescribing information (FPI) and highlights for pharmaceuticals and biological products through a regulation commonly referred to as the Prescription Labeling Rule (PLR). These standards have created a label that is more concise, easier to read and more accessible to electronic prescription methods.

A "quick reference" of the drug in the highlights of the FPI is a detailed snapshot of the most pertinent information practitioners and patients should be aware of. Both the FPI and highlights provide information and instructions that may pertain to the specific needs of the patient, with the what and how clearly articulated. The intent is for the drug to be more safely prescribed to a population for which it is intended, with additional details, if any, for those with special considerations.

While the full FPI for any drug should be reviewed thoroughly, following is an overview of the basics of drug labeling, as well as three key sections containing information of importance to specific populations.

Content Ordering

The FPI and highlights sections are laid out as mandated by the PLR, which contains 17 sections (see Prescription Label FPI Contents and Section Numbers). Should one or more of the 17 sections not pertain to a specific drug, they may be eliminated from the label; however, the sequential ordering of the sections must not be changed. For example, if there are no known drug interactions to be concerned with, section 7 may be omitted from the label, and the panel would move directly from section number 6 (adverse reactions) to section number 8 (use in specific populations).

Highlights and Boxed Warning

The highlights of a drug label are most often referred to; therefore, it is essential that the highlights provide immediate access to the most important information. Should the drug company determine more detailed information should be referenced beyond what is listed in the highlights, it may refer to and cross-reference other sections in the FPI that contain more detailed data.[1]

At the top of the highlights section is the boxed warning, critical information that the prescriber must be aware of. A boxed warning is also a required part of a label if the information is listed in the FPI. Boxed warnings inform consumers about possible adverse reactions to the drug that are so significant that the risks of the drug must be carefully weighed against the benefits. In the boxed warning, specific guidances for appropriate use to avoid those adverse reactions (such as specific monitoring, awareness of certain drug interactions and patient selection) and restrictions to ensure safe use are also included. Of special interest to providers is the inclusion of information specific to effective use in certain patient populations, if necessary. However, this information is usually found in the warnings and precautions section.[2]

Optional Content and Cross-Referencing

The only optional sections are the warnings and precautions, drug interactions and use in specific populations, though FDA highly recommends including warnings and precautions. The recent major changes section is required only if there are changes to the boxed warning, indications and usage, dosage and administration, contraindications or warnings and precautions, since these important updates must be conveyed.[3]

Prescribers should also be aware that section 2, dosing and administration, may be cross-referenced in any number of sections if the information may alter the dose. For instance, if a provider monitors for any specific therapeutic blood levels or metabolites for adverse events (section 6), if there are any details of the dosage with regard to specific populations (section 8), or if there are any specific drug interactions of concern due to concomitant medications (section 7), that information must be explained in multiple sections as needed.

Dosage and Administration

The dosage and administration section of the FPI contains subsections that are invaluable to prescribers of patients with special needs. Subsections include:

- Instructions for monitoring to assess effectiveness
- Monitoring to assess safety
- Monitoring therapeutic blood levels
- Dosage modifications because of drug interactions
- Dosage modifications for specific patient populations
- Important considerations concerning compliance with a dosage regimen

Prescription Label Full Prescribing Information Contents and Section Numbers

Boxed Warning
1 Indications and Usage
2 Dosage and Administration
3 Dosage Forms and Strengths
4 Contraindications
5 Warnings and Precautions
6 Adverse Reactions
7 Drug Interactions
8 Use in Specific Populations
- 8.1 Pregnancy
- 8.2 Labor and Delivery
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use

9 Drug Abuse and Dependence
- 9.1 Controlled Substance
- 9.2 Abuse
- 9.3 Dependence

10 Overdosage
11 Description
12 Clinical Pharmacology
- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics
- 12.4 Microbiology (by guidance)
- 12.5 Pharmacogenomics (by guidance)

13 Nonclinical Toxicology
- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

14 Clinical Studies
15 References
16 How Supplied/Storage and Handling
17 Patient Counseling Information

Source: Selected Requirements of Prescribing Information. Accessed at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/UCM373025.pdf.

All of these subsections paint a detailed picture for occurrences such as when to anticipate possible side effects in certain patients, how to adjust the drug therapy to help eliminate side effects, when to return to normal dosing and how to adjust the dosage in the future.

The dosage and administration section also gives information to help providers and patients understand the importance and the reason for any additional instructions. If there are reasons for compliance with specific instructions such as timing of the dosage or instructions for taking complex dosage forms, or if there are specific infusion administration details and possible reactions, that information is explained.[4]

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Adverse Reactions

FDA labels require the inclusion of only those adverse reactions for which there appears to be a direct causal link to the drug or drugs in the same pharmacologically active and chemically related class. The adverse reactions are arranged by body system, severity of reaction and in order of decreasing frequency. Those reactions with clinically severe implications will also be cross-referenced in other sections, as appropriate, such as the boxed warning, warnings and precautions and contraindications sections.

These reactions are also further separated by those reported during clinical trials and by both foreign and domestic post-marketing spontaneous reports. Post-marketing reports include a statement that helps practitioners understand the significance of any data.

It is important to note the distinction between adverse reactions and adverse events. Adverse reactions are those that have a causal relation between the use of the drug and the adverse event. Drug labels may also contain serious adverse events if those events have an unlikely occurrence in the absence of the drug therapy.[5]

Use in Specific Populations

This optional section is of special importance to providers because it provides details on any clinically significant differences in response or usage by population. Should there be detail for multiple populations, those populations must be listed in the same order in the highlights section and the FPI. While this section is optional and may be omitted in cases where there is no available data, sometimes that lack of data in and of itself is important if the drug has not been evaluated in certain populations. In those cases, this section should be retained with this detail included.

It should be noted that information regarding use of the drug by pregnant women is not included in the highlights section because FDA recommends instead a conversation between the provider and patient that includes all available data. However, any pertinent details on a drug's use during pregnancy are to be included in the FPI under subcategory 8.1: pregnancy.[6]

More Information Is Available

While this is merely a brief overview of what the information on drug labels includes, a more thorough review of all labeling details can be found on both FDA's website at www.fda.gov and on the drug manufacturer's website. Any serious adverse events should be reported to FDA's Medwatch at www.fda.gov/Safety/MedWatch/HowToReport/default.htm.

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References

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