Patient Counseling Information Section of Labeling for Human Prescription Drug and Biological Products — Content and Format

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2014
Labeling

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Contains Nonbinding Recommendations

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Guidance for Industry[1]

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I. INTRODUCTION

This guidance is intended to assist applicants in developing the PATIENT COUNSELING INFORMATION section of labeling required under § 201.57(c)(18) (21 CFR 201.57(c)(18)). [2] The recommendations in this guidance are intended to help ensure that this section of labeling is clear, useful, informative, and to the extent possible, consistent in content and format.

This guidance is intended to assist applicants with the following:

- How to decide what topics to include in the PATIENT COUNSELING INFORMATION section
- How to present information in the PATIENT COUNSELING INFORMATION section
- How to organize the PATIENT COUNSELING INFORMATION section

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of Medical Policy in the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] This guidance applies to drugs, including biological products. For the purposes of this guidance, *drug product or drug* will be used to refer to human prescription drug and biological products that are regulated as drugs.

II. BACKGROUND

On January 24, 2006, FDA published a final rule that amended the requirements for the content and format of labeling for human prescription drug and biological products (commonly referred to as the *physician labeling rule* (PLR)).[3] This rule created a new required section in labeling entitled PATIENT COUNSELING INFORMATION (§ 201.57(c)(18)). The PATIENT COUNSELING INFORMATION section summarizes the information that a health care provider should convey to a patient (or caregiver when applicable) when a counseling discussion is taking place (e.g., a physician prescribing a drug during an office visit, a nurse providing discharge instructions at a hospital, or a pharmacist conveying information at a pharmacy). Under § 201.57(c)(18), the PATIENT COUNSELING INFORMATION section of labeling must contain the following:

- Information necessary for patients to use the drug safely and effectively.
- If applicable, reference to FDA-approved patient labeling; the full text of such patient labeling must be reprinted immediately following the full prescribing information (FPI) or, alternatively, accompany the prescribing information.

Before FDA published the final rule, labeling regulations required that any information necessary for patients to use the drug safely and effectively be presented under *Information for Patients*, a subsection of the PRECAUTIONS section of *old format* labeling.[4] By requiring a dedicated section for such information in the PLR format, FDA recognized the importance of health care providers' counseling of patients. As labeling in the *old format* is converted to the PLR format in accordance with the implementation schedule under 21 CFR 201.56(c), applicants with labeling that did not include an *Information for Patients* subsection must develop a PATIENT COUNSELING INFORMATION section unless the section is clearly inapplicable and omitted under § 201.56(d)(4) (21 CFR 201.56(d)(4)) (see section III of this guidance).

Because regulatory requirements for the PATIENT COUNSELING INFORMATION section are broadly worded and many different presentations have been used in labeling approved in PLR format, this guidance seeks to (1) provide recommendations on how to select information to include and (2) bring greater consistency to the content and format of the PATIENT COUNSELING INFORMATION section.

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[3] See the final rule "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" (71 FR 3922, January 24, 2006). This rule is commonly referred to as the *physician labeling rule* (PLR) because it addresses prescription drug labeling that is used by prescribers and other health care professionals. The requirements are found at 21 CFR 201.56 and 201.57.

[4] Prescription drug products not described under § 201.56(b)(1) are not subject to § 201.57(c)(18), but are subject to 21 CFR 201.80(f)(2) addressing the *Information for Patients* subsection. The term *old format* refers to labeling that meets the requirements at 21 CFR 201.56(e) and 201.80.

III. CONTENT

The PATIENT COUNSELING INFORMATION section is written for use by a health care provider to identify topics for a counseling discussion with the patient. Therefore, the content and presentation of information in the PATIENT COUNSELING INFORMATION section typically will differ from those in FDA-approved patient labeling (e.g., Patient Package Inserts, Medication Guides, and Instructions for Use). The PATIENT COUNSELING INFORMATION section should contain the most important information for providers to convey to patients for the safe and effective use of a drug. Consequently, all topics presented in the PATIENT COUNSELING INFORMATION section should typically be included in any FDA-approved patient labeling. Information in the PATIENT COUNSELING INFORMATION section and any FDA-approved patient labeling, along with the provider-patient conversation, are essential and complementary components for the safe and effective use of prescription drugs.

The intent of the PATIENT COUNSELING INFORMATION section is to identify topics for counseling discussions between health care providers and patients after a prescribing decision has been made. Other sections of the labeling contain the detailed information used by prescribers to fully assess the risks and benefits of a drug for an individual patient.

The PATIENT COUNSELING INFORMATION section is required in all labeling subject to § 201.57, including for drugs used in an inpatient setting or other health care setting, such as a clinic or a physician's office. In extremely rare circumstances, the section may be omitted if its inclusion would be clearly inapplicable (e.g., labeling for standard intravenous fluids) as allowed under§ 201.56(d)(4).

Requirements and recommendations for the content of the PATIENT COUNSELING INFORMATION section are presented below in sections III.A through C.

A. Reference to FDA-Approved Patient Labeling

Under § 201.57(c)(18), if a product has FDA-approved patient labeling (e.g., Patient Package Insert, Medication Guide, and Instructions for Use), such labeling must be referenced in the PATIENT COUNSELING INFORMATION section. The reference to patient labeling informs health care providers of the existence of approved patient labeling and should direct them to advise patients to read such labeling.

The reference statement should appear first in the PATIENT COUNSELING INFORMATION section and identify the type(s) of FDA-approved patient labeling. Recommended language for the reference statement includes:

- Advise the patient to read the FDA-approved patient labeling (Patient Information).[5]
- Advise the patient to read the FDA-approved patient labeling (Instructions for Use).

[5] In this reference statement, *Patient Information* is used instead of *Patient Package Insert* because *Patient Information* more clearly identifies the purpose of and audience for the information and is generally used as the title of the FDA-approved patient labeling that is appended to the end of the FPI.

- Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

- Advise the patient to read the FDA-approved patient labeling (Medication Guide).

- Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

If counseling for a particular product is typically directed to a caregiver rather than the patient, the statements can be modified accordingly.

B. Counseling Topics

Information in the PATIENT COUNSELING INFORMATION section typically focuses on major risks of the drug and, when appropriate, how the patient may mitigate or manage these risks. This section should also include, when appropriate, other patient-focused information relevant for providers to convey, such as critical administration instructions or unique storage and handling instructions. In addition, there may be other information that is important for the health care provider to convey to the patient, such as a common drug effect that does not pose a risk to patients but could be important because it may be worrisome or potentially affect compliance (e.g., cough from the use of angiotensin-converting enzyme inhibitors).

Not every risk discussed in labeling will always be included in the PATIENT COUNSELING INFORMATION section, and those present in the PATIENT COUNSELING INFORMATION section will typically be serious or otherwise clinically significant. Only those topics critical for safe and effective use of the drug and appropriate for a provider-patient discussion should be included. These would typically include the most important risks about which patients should be informed and those for which a patient may need to do something actionable (e.g., contact the prescriber, immediately discontinue the drug, or seek emergency medical care). Topics presented elsewhere in labeling that provide information relevant only for the prescriber or other health care provider should typically not appear in the PATIENT COUNSELING INFORMATION section. Examples include information pertinent to proper patient selection, an explanation of the interpretation of laboratory results, or issues related to proper drug administration in an inpatient setting.

1. Presentation of the Information

The PATIENT COUNSELING INFORMATION section should summarize each topic to facilitate discussion between a health care provider and a patient and should include the level of detail appropriate for a counseling discussion. This focus and level of detail is typically not the same as the discussion of the related topic or risk described elsewhere in the FPI. The information in the PATIENT COUNSELING INFORMATION section should not be presented simply as a list of risks from use of the drug, nor should the information be a repeat of entire paragraphs from elsewhere in the labeling. Only in very rare instances will an entirely new

concept be included in the PATIENT COUNSELING INFORMATION section that does not have a related discussion elsewhere in labeling.

Consistent with the approach used for other sections of labeling (e.g., BOXED WARNING, WARNINGS AND PRECAUTIONS), information in the PATIENT COUNSELING INFORMATION section should be ordered by the relative clinical significance of the information, with the most important topics applicable to the patient appearing first. For this reason the topics presented may or may not reflect the order in which they first appear overall in the FPI (i.e., within the PATIENT COUNSELING INFORMATION section, a topic from the WARNINGS AND PRECAUTIONS section may appear before a topic from the DOSAGE AND ADMINISTRATION section).

Information in the PATIENT COUNSELING INFORMATION section should typically be presented using active voice (e.g., "Advise the patient to…") rather than passive voice (e.g., "Patients should be advised to…") to provide clearer directives to the reader.

2. Types of Information to Consider for Inclusion

a. Important adverse reactions and other risks

The PATIENT COUNSELING INFORMATION section summarizes important adverse reactions and other risks to convey to patients. Information should typically include, as appropriate, the identification of the risk, management recommendations that are pertinent to patients, self-monitoring information, and information on when to contact a health care provider, seek emergency help, or discontinue the drug. For example:

> <u>Serious Allergic Reactions</u>
> Advise the patient to discontinue DRUG-X and seek immediate medical attention if any signs or symptoms of a hypersensitivity reaction occur *[see Warnings and Precautions (5.X)]*.

A listing of the most common adverse reactions should not be included in the PATIENT COUNSELING INFORMATION section. However, an individual common adverse reaction should be included if it is among the most important adverse reactions applicable to the patient (e.g., appears in WARNINGS AND PRECAUTIONS) or the risk of its occurrence is important to convey to a patient (e.g., urine discoloration from use of rifampin).

b. Contraindications

Although contraindications are essential for informing prescribing decisions, most are typically not appropriate for a patient counseling discussion that occurs once a prescribing decision has been made. Some contraindications, however, may warrant inclusion in the PATIENT COUNSELING INFORMATION section for conditions that may develop after starting drug therapy (e.g., development of an acute infection).

c. Drug interactions

Interactions or effects from other drugs or foods should be included in the PATIENT COUNSELING INFORMATION section if they concern an important risk (e.g., are mentioned in the BOXED WARNING, CONTRAINDICATIONS, or WARNINGS AND PRECAUTIONS sections). Additionally, an interaction should be included if coadministration could be initiated by the patient (e.g., an interaction with food or an over-the-counter drug or dietary supplement). A complete listing of known drug interactions should typically not be included in the PATIENT COUNSELING INFORMATION section because the decision to coadminister two prescription drugs generally rests with the provider at the time of prescribing.

In rare cases, a drug may have multiple serious drug interactions (e.g., warfarin or certain antiretroviral drugs) that would warrant a broadly worded recommendation in the PATIENT COUNSELING INFORMATION section to inform patients of the overall risk. A cross-reference would direct the health care provider to the more detailed discussion elsewhere in labeling.

d. Information on use in pediatric patients, pregnancy, and lactation

Consistent with the approach taken for drug interactions, include a discussion of the risks of a drug in pediatric patients, pregnancy, or during lactation should be included in the PATIENT COUNSELING INFORMATION section if the information concerns an important risk (e.g., is mentioned in the BOXED WARNING, CONTRAINDICATIONS, or WARNINGS AND PRECAUTIONS sections). If the drug has no such risk, general advice on the use of drugs in pediatric patients or during pregnancy or lactation (e.g., "Advise a female patient to inform the prescriber if she is pregnant or planning to become pregnant") should not be included in the PATIENT COUNSELING INFORMATION section (see Section III.C. Information Not to Include).

Additionally, if there is a pregnancy exposure registry mentioned in the *Pregnancy* subsection of the USE IN SPECIFIC POPULATIONS section, the availability of the registry should be included in the PATIENT COUNSELING INFORMATION section, with a cross-reference to the *Pregnancy* subsection where the contact information necessary to enroll may be found.

e. Information on preparation and administration

Full details on proper preparation and administration of a drug should typically appear in the DOSAGE AND ADMINISTRATION section, whereas the PATIENT COUNSELING INFORMATION section should summarize the most important points relevant to a counseling conversation. For example:

> Importance of Second Application
> Inform the patient that the second application of DRUG-X is necessary to kill any live lice that hatch following the initial treatment *[see Dosage and Administration (2.X)]*.

In general, the PATIENT COUNSELING INFORMATION section should not include typical dosage regimen information (e.g., instructions to take one 30 mg tablet every 12 hours) for drugs that are self-administered by the patient. However, pertinent advice on how to self-administer should be briefly summarized if there are specific instructions for administration that need to be followed so that the drug is used safely and effectively. Specific information may include instructions to take the drug with a high-fat meal or on an atypical dosing schedule (e.g., tapered dosing of prednisone). For example:

> Administration Instructions
> Advise the patient to swallow DRUG-X capsules intact and not to open, chew, or crush the capsules. Inform the patient that the nonabsorbable DRUG-X capsule shell may be visible in the stool.

If a product has FDA-approved patient labeling that includes details on self-administration (e.g., Instructions for Use), the detailed information should not be repeated verbatim in the PATIENT COUNSELING INFORMATION section. The reference statement appearing at the beginning of the PATIENT COUNSELING INFORMATION section directs health care providers to advise patients to read the FDA-approved patient labeling.

For self-administered injectable drugs, information regarding proper sharps disposal will typically be included in the FDA-approved Instructions for Use. The PATIENT COUNSELING INFORMATION section should include a statement directing providers to advise patients to follow sharps disposal recommendations,[6] but should not summarize or repeat the information found in the Instructions for Use.

f. Products with restricted distribution as a component of a Risk Evaluation and Mitigation Strategies (REMS) program

Reference the to the existence of a REMS program that includes restricted distribution should be included in the PATIENT COUNSELING INFORMATION section along with a brief description of only those program elements that directly impact the patient (e.g., a requirement to enroll in the program or the availability of the drug only from pharmacies participating in the program). If no elements of restricted distribution directly impact patients, information regarding the REMS program should not appear in the PATIENT COUNSELING INFORMATION section.

g. Instructions related to storage and handling

In rare cases, there may be important, atypical storage or handling information appropriate for a provider-patient discussion that should be included in the PATIENT COUNSELING INFORMATION section. For example:

[6] Information about safe disposal of needles and other sharps outside of health care settings is available on the Internet at http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/HomeHealthandConsumer/ConsumerProducts/Sharps/default.htm.

Handling Instructions
Advise the patient that females of reproductive potential should not handle broken or crushed DRUG-X tablets because DRUG-X may cause harm to a male fetus *[see Warnings and Precautions (5.X)]*.

As with preparation and administration instructions, the same topics may be discussed in the PATIENT COUNSELING INFORMATION section, the HOW SUPPLIED/STORAGE AND HANDLING section, and in the FDA-approved patient labeling regarding proper storage and handling, but the focus of the discussion should reflect the intent of the section of labeling in which the information resides.

h. Additional requirements

Certain products have additional, specific requirements for the PATIENT COUNSELING INFORMATION section based on the product's therapeutic or pharmacologic class (e.g., 21 CFR 201.24(d) for systemic antibacterial drug products).

C. Information Not to Include

Not all information related to use of a drug should be included in the PATIENT COUNSELING INFORMATION section. The PATIENT COUNSELING INFORMATION section is intended to facilitate the provider-patient discussion, but is not intended to serve as a script for the provider.

Examples of information that should generally ***not*** be included in the PATIENT COUNSELING INFORMATION section include the following:

- Indication or use of a drug
- General recommendations lacking context that would be considered a standard component of any provider-patient discussion (e.g., "Discuss the risks and benefits of DRUG-X")
- General advice that could apply to any drug (e.g., "Instruct the patient to keep DRUG-X out of reach of children") unless particularly relevant for an individual product (e.g., the need to keep opioid-containing patches away from children and pets)
- Information that informs prescribing decisions (e.g., "DRUG-X is contraindicated in patients with a history of thromboembolic events")
- Routine administration or storage and handling information that would typically be conveyed to the patient at the time of dispensing (e.g., the need to shake an oral suspension before use or to store it in the refrigerator at home)

- Definitions or descriptions of medical terminology (e.g., a listing of signs and symptoms of neuroleptic malignant syndrome, a potential serious adverse reaction from the use of antipsychotic drugs) that need not be explained to a health care provider audience

- Graphics (e.g., illustrations or pictures related to administration)

IV. FORMAT

The PATIENT COUNSELING INFORMATION section is subject to the applicable formatting requirements under §§ 201.56(d) and 201.57(d). Additional recommendations are presented below in sections IV.A through C.

A. Subheadings

Following the required reference to any FDA-approved patient labeling, information in the PATIENT COUNSELING INFORMATION section should be presented in a consistent format that enhances its readability and usefulness. The use of subheadings to organize and differentiate topics within the PATIENT COUNSELING INFORMATION section is recommended because they allow the reader to quickly identify the major concepts. Subheading titles should clearly identify the focus of each discussion (e.g., Acute Hepatic Failure rather than simply Hepatic), and a consistent formatting of the subheading titles (e.g., underlining or italicizing) is recommended.

Because the content presented about each topic is generally one or two short statements, numbered subsections (e.g., 17.1, 17.2) are typically unnecessary and are not recommended. Moreover, numbered subsections cause unnecessary length and clutter in both the PATIENT COUNSELING INFORMATION and in Contents (§ 201.57(b)) and may be redundant with subsection titles elsewhere in the labeling (e.g., the WARNINGS AND PRECAUTIONS section).

B. Cross-Referencing

Because information under the PATIENT COUNSELING INFORMATION section typically summarizes information presented elsewhere in the labeling, cross-referencing should be used to direct the reader to the more detailed discussion. If, however, the other section of the labeling where the related topic is discussed contains no more information than appears in the PATIENT COUNSELING INFORMATION section, no cross-reference is necessary.

C. Appending FDA-Approved Patient Labeling

If FDA-approved patient labeling immediately follows the FPI, the FDA-approved patient labeling should not be assigned a subsection number and should instead be separated from the FPI by other formatting techniques (e.g., a horizontal line or page break).