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Draft Guidance on the Indications and Usage Section of Labeling

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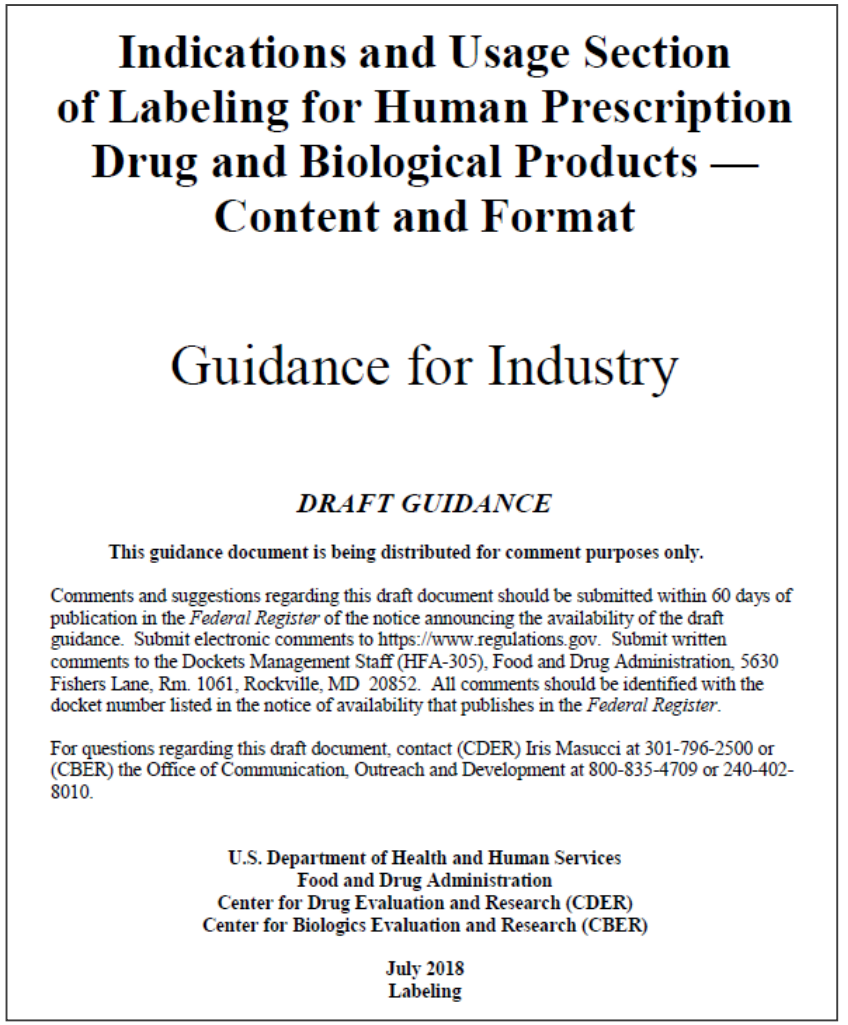

Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products — Content and Format

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Iris Masucci at 301-796-2500 or (CBER) the Office of Communication, Outreach and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
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Topics in the Indications & Usage draft guidance

- General principles to consider when drafting the Indications & Usage (I&U) section
- What information to include in the I&U section
- When to include additional descriptors or qualifiers as part of the indication in the I&U section
- When to include limitations of use in the I&U section
- How to write, organize, and format the information within the I&U section

Indications & Usage section of labeling

- Primary role is to enable health care practitioners to readily identify appropriate therapies for patients by clearly communicating the drug's approved indication(s)
- Should be clear, concise, useful, and informative and, to the extent possible, consistent within and across drug and therapeutic classes

Scope of an indication relative to the population studied

- I&U section should clearly communicate the scope of the approved indication, including the population to which the determination of safety and effectiveness is applicable
- Indicated population may mirror the studied population (e.g., in terms of patient demographics or severity of disease or condition), but can sometimes differ

Broader than studied

- An indication for a broader population than the patient population studied in controlled trials may be appropriate after careful consideration of:
  - Generalizability of the evidence
  - Consistencies in the disease process across different groups
  - Drug's overall benefits and risks

Broader than studied

- Indications cover patient populations that were absent or specifically excluded from the clinical studies supporting approval
  - e.g., geriatric patients, pregnant women, patients taking certain concomitant drugs, patients with a different severity or stage of a disease

Example of a broader indication

- A study evaluating a drug in adults enrolled patients of a certain age range and excluded patients taking certain concomitant drugs
- Available evidence does not suggest the drug would be unsafe or ineffective in adult patients outside that age range or in those taking the other drugs

Indication should be worded to reflect a broader age group (i.e., “in adults”), rather than the exact ages studied. And unless available evidence suggests otherwise, the indication should not exclude use in patients taking the concomitant drugs.

Example of a narrower indication

- A study enrolled and randomized patients, but then also stratified participants by the presence or absence of a specific genomic marker
- The study demonstrated benefit only in patients who had tested positive for the marker

FDA may conclude that the available evidence supports approval of an indication in a population that is narrower in scope than the population that was studied.

Pediatric considerations

- Approach noted earlier about generalizing among adult populations is generally not appropriate across pediatric populations or between adult and pediatric populations because of:
  - Statutory requirements related to pediatric assessments
  - Unique clinical considerations for pediatric patients (e.g., pediatric patients may metabolize drugs differently from adults, are susceptible to different safety risks, and often require different dosing regimens, even after correction for weight)

Inclusion of age groups in indications

An indication should state that a drug is approved, for example:

- “in adults”
- “in pediatric patients X years of age and older”
- “in adults and pediatric patients X years of age and older”

Content and format of the I&U section

The I&U section includes:

- the indication
- and, as appropriate, any identified limitations of use

Details to include in the indication

- For many drugs, the indication will be sufficiently conveyed by stating the disease or condition being treated, prevented, mitigated, cured, or diagnosed, and the approved age group(s)
- In such circumstances, endpoints and descriptions of benefit should be summarized in the CLINICAL STUDIES section of labeling and should not be included in the indication

Details to include in the indication

- However, other scenarios may warrant the inclusion of more information in the indication.
- For example:
  - When a drug may target different aspects of a disease (e.g., in multiple sclerosis)
  - When endpoints are not well-standardized (e.g., in heart failure)

In these scenarios, the specific benefits of the drug should be stated within the indication.

Example of endpoints within indications

- For a drug indicated for the treatment of insomnia, the indication should state whether the drug affects sleep onset, sleep maintenance, or both, in order to facilitate appropriate prescribing for an individual patient
- For many outcome studies, when there is an overall effect on a composite endpoint, the indication should identify the components of the composite (e.g., cardiovascular death, myocardial infarction, and stroke)

Components of the indication

The indication should begin “DRUG-X is indicated” and must include the following elements required under 21 CFR 201.57(c)(2)(i):

- The disease, condition, or manifestation of the disease or condition (e.g., symptoms) being treated, prevented, mitigated, cured, or diagnosed
- When applicable, other information necessary to describe the approved indication

Selected patient subgroups

- DRUG-X is indicated for the treatment of adult and pediatric patients 12 years of age and older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Adjunctive or concomitant therapies

- DRUG-X is indicated in adults for the treatment of high-grade malignant glioma as an adjunct to surgery and radiation.

Specific tests needed for proper patient selection

- DRUG-X is indicated for the treatment of adult patients with metastatic non-small cell lung cancer whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Overview of “limitations of use”

Are included when:

- The evidence falls short of requiring a contraindication, but suggests that use of the drug may be inadvisable
- There is sufficient uncertainty about the drug’s benefits in certain clinical situations to suggest that the drug should generally not be used in those settings
- The awareness of such information is important for practitioners to ensure the safe and effective use of the drug

Reasonable concern or uncertainty about effectiveness or safety in a certain clinical situation

DRUG-X is indicated for the treatment of hypertension in adults and pediatric patients 1 year of age and older.

Limitations of Use

In patients younger than one year of age, DRUG-X can adversely affect kidney development *[see Warnings and Precautions (5.X) and Use in Specific Populations (8.4)].*

Drugs with dose, duration, or long-term use considerations

DRUG-X is indicated for the treatment of severe spasticity in adult patients with spinal cord injury, brain injury, or multiple sclerosis.

Limitations of Use

Prior to implantation of a device for chronic intrathecal infusion of DRUG-X, confirm a positive clinical response to DRUG-X in a screening phase *[see Dosage and Administration (2.X)]*.

Do not use LOUs…

- To restate information already included in the indication
  - e.g., if an indication is clearly worded for use in combination with another drug, there is no need for a limitation of use stating that the subject drug should be used only in combination and not as monotherapy

Do not use LOUs…

- To address an absence of data in populations in which the drug was not studied
  - e.g., if a drug is approved to reduce the risk of rejection in patients receiving a heart transplant, there should not be a limitation of use about the lack of data on use in lung transplants

Format for multiple indications

- Can assign a subsection to each indication

  1.1 DiseaseA

  1.2 DiseaseB

- Can present distinct indications using bullets

  DRUG-X is indicated for:

  -
  -

Format for limitations of use

- Presented separately from the indication within I&U under the heading *Limitations of Use* and not usually under a separate numbered subsection
- If a drug has multiple indications and the LOU applies to all of them, it may be preferable to use a separate numbered subsection for *Limitations of Use* within the section

Thank You

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