Regulatory Education for Industry (REdI): PRESCRIPTION DRUG LABELING - CHALLENGES AND ISSUES

Bethesda Marriott | Pooks Hill, MD | November 3-4, 2015

Distributing Specific Population Information in Labeling

Eric Brodsky, M.D.
Associate Director, Labeling Development Team
Office of New Drugs, Center for Drug Evaluation and Research
Food and Drug Administration (FDA)

Disclaimer

- The views and opinions expressed in this presentation represent those of the presenter, and do not necessarily represent an official FDA position.
- The labeling examples in this presentation are fictitious and are provided only to demonstrate current labeling development challenges.

Distribution of Renal Impairment Information: Example Overview

2 DOSAGE AND ADMINISTRATION

The recommended once daily oral dosage of DRUG-X is:

- 25 mg in patients with normal renal function or mild renal impairment (i.e., creatinine clearance between 60 to 90 mL/minute as estimated by Cockcroft-Gault).
- 12.5 mg in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute as estimated by Cockcroft-Gault) *[see Use in Specific Populations (8.6)].*

8 USE IN SPECIFIC POPULATIONS

8.6 Renal Impairment

The use of DRUG-X in patients with moderate or severe renal impairment was associated greater blood levels of drugoxide compared to patients with normal renal function *[see Clinical Pharmacology (12.3)].* Given that increased drugoxide blood levels increases the risk of Adverse Reaction-Y, a dosage reduction in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute) is recommended *[see Dosage and Administration (2)].* A dosage reduction in patients with mild renal impairment is not needed.

12 CLINICAL PHARMACOLOGY

12.3 Pharmacokinetics

Specific Populations

Patients with Renal Impairment: Compared to patients with normal renal function, the AUC of drugoxide was increased X%, Y%, Z% in patients with mild renal impairment [creatinine clearance (Clcr) 60 to 90 mL/minute], moderate renal impairment (Clcr 30 to 60 mL/minute), and severe renal impairment (Clcr less than 30 mL/minute), respectively, following a single 25 mg dose of drugoxide In addition, the Cmax of drugoxide was increased A%, B%, C% in patients with mild, moderate, and severe renal impairment, respectively *[see Dosage and Administration (2) and Use in Specific Populations (8.6)].*

Distribution of Renal Impairment Information Example: Subsection 12.3

12 CLINICAL PHARMACOLOGY
12.3 Pharmacokinetics

Specific Populations

Patients with Renal Impairment: Compared to patients with normal renal function, the AUC of drugoxide was increased X%, Y%, Z% in patients with mild renal impairment [creatinine clearance (Clcr) 60 to 90 mL/minute], moderate renal impairment (Clcr 30 to 60 mL/minute), and severe renal impairment (Clcr less than 30 mL/minute), respectively, following a single 25 mg dose of drugoxide In addition, the Cmax of drugoxide was increased A%, B%, C% in patients with mild, moderate, and severe renal impairment, respectively *[see Dosage and Administration (2) and Use in Specific Populations (8.6)].*

- Develop data subsections before clinical subsections
- Describe PK studies and results conducted to identify PK differences in patients with varying degrees of renal impairment relative to PK of drug in patients with normal renal function*

* Section IV(C)(4) - Clinical Pharmacology Section of Labeling Guidance; Section VI(F) - PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance

PK = pharmacokinetics

Distribution of Renal Impairment Information Example: Subsection 8.6

8 USE IN SPECIFIC POPULATIONS

8.6 Renal Impairment

The use of DRUG-X in patients with moderate or severe renal impairment was associated greater blood levels of drugoxide compared to patients with normal renal function *[see Clinical Pharmacology (12.3)]*. Given that increased drugoxide blood levels increases the risk of Adverse Reaction-Y, a dosage reduction in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute) is recommended *[see Dosage and Administration (2)]*. A dosage reduction in patients with mild renal impairment is not needed.

- Describe clinical implications of differences in response, safety, or recommendations for use of drug in patients with renal impairment compared to patients with normal renal function*

* Section VI(D) - PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance

Distribution of Renal Impairment Information Example: Section 2

2 DOSAGE AND ADMINISTRATION

The recommended once daily oral dosage of DRUG-X is:

- 25 mg in patients with normal renal function or mild renal impairment (i.e., creatinine clearance between 60 to 90 mL/minute as estimated by Cockcroft-Gault).
- 12.5 mg in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute as estimated by Cockcroft-Gault) *[see Use in Specific Populations (8.6)]*.

- Must include dosage modifications in D&A section for specific populations*
- Should include method for calculating creatinine clearance**

* 21 CFR 201.57(c)(3)(H); Section II(F) – D&A Section of Labeling Guidance

** Section VI(B) - PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance

References

- PLR Requirements for Prescribing Information website: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm

- PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM204959.pdf

Thank you!