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Rx package inserts: Redesigned with fewer errors in mind

The first PI makeover in 25 years adds "highlights" and adverse event hotlines

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The package insert (PI) is getting an FDA-mandated "makeover"—one that should make it faster and easier to locate the piece of information you need before writing a prescription.

PIs for newly approved drugs will now feature a *Highlights* section at the top, a *Contents* section to help you find what you're looking for, and a *Patient Counseling* section. Also new: manufacturer and FDA contact information near the top of the PI to facilitate adverse drug reaction reporting (**FIGURE**).

These revisions—the first that the FDA has mandated for the PI in 25 years[1]—are designed to save time and reduce adverse drug events. Evidence suggests that physicians could save approximately 15 seconds each time they refer to the new PI, thereby increasing the extent to which prescribing information is consulted.[2]

Additionally, the FDA anticipates healthcare system savings of approximately $400 million in the next 10 years resulting from adverse drug events avoided,[2] presumably because prescribers will be better informed. The new format should also help increase adverse drug reaction reporting by providing toll-free contact information.[3]

Lack of Rx information caused many mistakes

Changing the PI became an FDA priority in 2000, after the Institute of Medicine (IOM) published its report, "To err is human: Building a safer health system."[4] In this report, the IOM indicated that medication errors accounted for almost 98,000 deaths annually and that some of these deaths were a result of confusing medical information.[4] A July 2006 IOM report estimated that there are at least 1.5 million preventable adverse drug events resulting from medication errors in the US each year.[5]

One study demonstrated that the most common cause of medication errors was a lack of drug information at the time the prescription was written, resulting in 22% of the errors.[6] A subsequent report released by the IOM in September 2006 identified the importance of improving the FDA's role in monitoring drug safety in the postmarketing stage and conveying the risks and benefits of medications to the public.[7]

To help address this growing list of concerns, the FDA issued new regulations for the PI format in January 2006.[1] Among its goals: Prompt pharmaceutical companies to create PIs that read more like a drug information reference, and less like a sophisticated legal document.

CONTINUED

FIGURE

The package insert's new look[13]

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use JANUVIA safely and effectively. See full prescribing information for JANUVIA.

JANUVIA™ (sitagliptin) Tablets
Initial U.S. Approval: 2006

----------INDICATIONS AND USAGE----------
JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus (type 2 diabetes). JANUVIA is indicated for:

- Monotherapy (1.1)
- Combination therapy with metformin or a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (e.g., thiazolidinediones) when the single agent does not provide adequate glycemic control. (1.2)

Important Limitations of Use: JANUVIA should not be used in patients with type 1 diabetes mellitus (type 1 diabetes) or for the treatment of diabetic ketoacidosis. (1.3)

----------DOSAGE AND ADMINISTRATION----------
The recommended dose of JANUVIA is 100 mg once daily as monotherapy or as combination therapy with metformin or a PPARγ agonist (e.g., thiazolidinediones). (2.1)

JANUVIA can be taken with or without food. (2.1)

Dosage Adjustment in Patients With Moderate, Severe and End Stage Renal Disease (ESRD) (2.2)	
50 mg once daily	25 mg once daily
Moderate CrCl ≥30 to <50 mL/min ~Serum Cr levels [mg/dL] Men: >1.7– ≤3.0; Women: >1.5– ≤2.5	Severe and ESRD CrCl <30 mL/min ~Serum Cr levels [mg/dL] Men: >3.0; Women: >2.5; or on dialysis

----------DOSAGE FORMS AND STRENGTHS----------
Tablets: 100 mg, 50 mg, and 25 mg (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
A dosage adjustment is recommended in patients with moderate renal insufficiency and in patients with severe renal insufficiency or with ESRD requiring hemodialysis or peritoneal dialysis. Assessment of renal function is recommended prior to initiation of JANUVIA and periodically thereafter. Creatinine clearance can be estimated from serum creatinine using the Cockcroft-Gault formula. (2.2, 5)

----------ADVERSE REACTIONS----------
The most common adverse reactions, reported in ≥5% of patients treated with JANUVIA and more commonly than in patients treated with placebo are: upper respiratory tract infection, nasopharyngitis, and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck & Co., Inc. at 1-877-888-4231 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------USE IN SPECIFIC POPULATIONS----------
Safety and effectiveness of JANUVIA in children under 18 years have not been established. (8.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2007

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

New PI makes its way online

As PIs are revised to comply with the new regulations, the information in them will be used to populate a new online drug resource for clinicians (and the public) known as DailyMed.[9] This free, online health information clearinghouse, developed by the FDA and National Library of Medicine, can be found at dailymed.nlm.nih.gov/dailymed/about.cfm. It's intended to provide wide access to prescribing information for physicians at the point of care.[9] DailyMed features approved prescribing information, adverse event reporting information, and links to clinical articles.[3,9] Additionally, DailyMed provides access to MedlinePlus, an online medication tool for consumers written in lay language.[9]

FAST TRACK

You can find what you're looking for quickly in the new *Contents* section

The new FDA regulations apply to all New Drug Applications (NDAs), supplemental NDAs, and Biologics License Applications (BLAs) submitted on or after June 30, 2006.[1] In addition, drugs approved in the 5 years prior to the effective date, and older drugs for which there is a major change in the prescribing information (ie, new indication), will need to adopt the revised format over the next several years.[2,8] Medications that are exempt from these requirements include over-the-counter products, generic drugs, and existing drugs with minor labeling changes.

To get the word out to the healthcare community, the FDA and Institute for Safe Medication Practices kicked off a national educational campaign last fall by providing an overview of the new labeling format during a live teleconference.[8] In addition, this PI information is being posted on the Web. (See **"New PI makes its way online"**[3,9] above.)

Immediate access to important information

The revised PI contains 3 new sections: *Highlights*, *Contents*, and *Patient Counseling Information*.[10]

Highlights. The *Highlights* section is the most significant change to the PI, and provides immediate access to the most important prescribing information.[1,11,12] It's displayed prominently at the top of the PI and is a concise half-page summary that includes references to detailed sections in the *Full Prescribing Information*.[2,3]

The *Highlights* section is analogous to a structured abstract in a published clinical trial (**FIGURE**).[13] It contains recent major changes to the following sections: *Boxed Warning*, *Indications and Usage*, *Dosage and Administration*, *Contraindications*, and *Warnings and Precautions*.[12] Additionally, the original FDA drug approval date of the product is listed, enabling physicians to easily identify new medications.[2,3] Manufacturer and FDA contact information is also provided to encourage and facilitate adverse drug reaction reporting.[12]

Contents. Physicians will be able to locate information more quickly with the *Contents* section. This section, which is analogous to the table of contents of a book, references all sections and subsections in the *Full Prescribing Information section*.[12]

Patient counseling. The new format now requires a Patient Counseling Information section that places a greater emphasis on the importance of communication between physicians and patients. This section provides key points, including information on dosing instructions, laboratory tests, and drug safety. This section is designed to help physicians by providing efficient and concise talking points involving drug usage.[1]

New design bids laundry lists farewell

The overall structure of the PI has been revised to allow easier access to important information and to group related sections.[3] Information physicians frequently consult and consider most critical (ie, *Boxed Warnings*, *Indications and Usage*, *Dosage Forms and Strengths*, *Dosage and Administration*) are located at the beginning.[3,12]

The *Adverse Reactions* section no

longer contains a laundry list of adverse reactions and is divided into 2 parts: clinical trials experience (adverse events identified during clinical trials) and postmarketing experience (adverse events reported spontaneously by physicians and patients).[8] Additionally, the *Warnings and Precautions* are now consolidated into 1 section instead of being listed separately.[8]

The new regulations also require that the PI text be formatted in a certain way. The FDA requires that certain elements be in bold, and that there be a minimum font size to enhance the communication of important information.[2,3] (Previously, there was no minimum font size requirement.) Type in the PI can now be no smaller than 6 points and labeling on promotional materials and product samples can be no smaller than 8 points.

Manufacturers worry that details will be overlooked

Manufacturers have expressed concern over the addition of the *Highlights* section to the PI, noting that physicians might rely too heavily on the condensed information when making prescribing decisions.[2,14] Manufacturers are also concerned that they will be forced to choose certain information for the *Highlights* section while excluding other valuable points, increasing their liability.[2,14] The FDA, though, seems to have addressed this issue: The *Highlights* section includes a limitation statement emphasizing that physicians should still refer to the complete prescribing information.[2,14]

Another concern: The revisions to the PI come at a price, albeit a relatively small one. Updating the PI is expected to cost manufacturers approximately $6190 for each new product and $8700 for each existing product.[2]

Overall, though, the revisions to the PI should lead to positive change by providing physicians with access to up-to-date information in a clear, concise, and easy-to-read format. Though not a panacea for medication errors, the new PI should serve as an improved tool in the physician's arsenal. ■

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Disclosure
No potential conflict of interest relevant to this article was reported.

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FAST TRACK

Spotting adverse events that have been reported by physicians and patients is now easier