Consistency of Publicy-Accessible Generic Drug Labels with Reference Listed Drug Labels in DailyMed: A Case Analysis for the Special Populations

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RESULTS

Exhibit 1: Percentage of Generic Drug Labels With/Without a Difference when Compared to the Brand Drug Label Listed in DailyMed

Label Section	Total Number of Generic Drug Labels Reviewed	Generic Drug Labels with NO Difference in Any Label Section	Generic Drug Labels with MINOR Differences in This Section	Generic Drug Labels with MAJOR Differences in This Section
Information for Patients	101	27%	4%	68%
Labor and Delivery	62	79%	2%	19%
Nursing Mothers	97	81%	0	19%
Pediatric Use	92	68%	1%	30%
Geriatric Use	102	75%	1%	25%
Pregnancy	91	38%	1%	61%
Use in Specific Populations	80	71%	1%	28%

Exhibit 2: Consistency of Information on Special Populations in Generic Drug Labels with One or More Differences in a Label Section Listed in DailyMed

Label Section	Number of Generic Drug Labels with a MAJOR Difference	Information on Special Population was CONSISTENT Between Brand and Generic Drug Label	Information on Special Population was INCONSISTENT Between Brand and Generic Drug Label
Information for Patients	**69**	49%	51%
Labor and Delivery	**12**	0	100%
Nursing Mothers	**18**	11%	89%
Pediatric Use	**28**	46%	54%
Geriatric Use	**25**	76%	24%
Pregnancy	**56**	47%	53%
Use in Specific Populations	**22**	59%	41%

Exhibit 3: Examples of Inconsistent Information Between the Brand and Generic Drug Label Listed in DailyMed

Brand Drug Label	Generic Drug Label
"the effect of Abilify on labor and delivery is unknown"	Information about use in pregnancy was not present on the generic label section
"..no dosage adjustment for Abilify is required on the basis of a patient's sex, race or smoking status… "	"..dosage adjustment is recommended in CYP2D6 poor metabolizers due to high aripiprazole concentrations…. Required on the basis of a patient's hepatic function, renal function..."
"..pregnancy category C… Neoral should not be used in pregnancy unless the potential benefit to the mother justifies the potential risk to the fetus..."	pregnancy warnings, not present on generic drug label section
Information on renal insufficiency not on the brand drug label section	"..dosage adjustment in adult patients with compromised renal function is necessary. Pediatric patients with renal insufficiency have not been studied. Dosage adjustment in patients undergoing hemodialysis is necessary."

BACKGROUND

Bioequivalence studies that compare a reference formulation to an investigational generic formulation typically are conducted in healthy adult volunteers and occasionally are conducted in patients. Some populations have unique physical, biological, and physiological considerations that are not reflected by healthy volunteers or by the typical patient for whom a drug is indicated. It is important to evaluate the drug labeling specific to these special populations to identify potential barriers to generic substitution. Five special populations were the focus of this study, and include pediatric patients, women, older adults, racial/ethnic minorities, individuals with impaired kidney or liver function.

OBJECTIVES

To evaluate labels of 11 drugs to assess whether information on drug administration in special populations under study is documented consistently between brand-name and AB-rated generic drugs. Drugs with narrow therapeutic indices (NTI), and non-NTI drugs used "off-label" in special populations were selected and include: aripiprazole, cyclosporine, escitalopram, gabapentin, levothyroxine, mycophenolate mofetil, olanzapine, quetiapine, risperidone, tacrolimus, and valproic acid.

METHODS

- Extracted the drug label sections (using LOINC codes) from the drug labels (in XML format) from DailyMed[1] and converted to CSV/Excel files.
- Concatenated the labels by drug. Each label was identified by the label holder.
- Used the FDA Orange Book to exclude label holders that were not listed as an NDA or ANDA applicant (i.e., exclude labels from repackages).
- Compared 7 label sections from the label of the NDA holder to the corresponding section in the label of the ANDA holder.
- The 7 drug label sections reviewed are: Information for Patients; Labor and Delivery; Nursing Mothers; Pediatric Use; Geriatric Use; Pregnancy, Use in Specific Populations
- Differences that do not convey the same information in the NDA label were defined as major, e.g., when partial or entire content of a section was missing. Minor differences include differences due to the availability of different doses, or reference to the brand name vs. generic name of a drug.

CONCLUSIONS & LIMITATIONS

- Majority of generic drug label sections showed no differences.
- Minor differences could be attributed to patent exclusivity and other permissible differences.
- Drug administration information directed at special populations was not always presented consistently across all seven label sections for the 11 drugs reviewed.
- The combination of proactive monitoring and innovative technologies are needed to enable ongoing label compliance.
- Limitations:
  - DailyMed contains labeling information submitted by manufacturers and includes recent updates that may be pending FDA's review. It also may contains outdated NDA label that is different from the one list at Drugs@FDA
  - There may be differences in the timeliness of updates of the brand and generic drug labels.

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[1]DailyMed is provided by the National Library of Medicine (NLM). The drug labeling information on this Web site is the most recent submitted to the Food and Drug Administration (FDA): https://dailymed.nlm.nih.gov/dailymed/index.cfm