Post-marketing Surveillance of Generic Drug Usage and Substitution Patterns

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Introduction

- State laws and health insurance policies promote generic substitution as an important and effective tool to reduce prescription drug costs
- Generic substitution is based on bioequivalence (BE), but there are situations where the traditional *in vivo* pharmacokinetic BE studies may not be the appropriate method to ensure therapeutic equivalence
- Increasing availability of complex generic products and varied BE methods have led to controversy surrounding the approval process for some generic drugs (e.g. citizen petitions)
- Despite economic incentives, patient and physician concerns about generics may result in avoiding generic substitution or switching back to the brand name drug from the generic drug

Objectives

- To conduct an analysis of administrative claims to estimate generic and brand medication utilization, switching, and switchback rates
- To compare utilization patterns of generic drugs approved with conventional and controversial BE study designs

Methods

- Data source: Medicare administrative and Part D prescription drug event data for a 5% random sample of Medicare beneficiaries (2006 - 2009)
- Cohort eligibility criteria: ≥1 prescription for brand product from 6 months prior to index date through 12/31/2009; a minimum follow up was not required; complete coverage for Medicare Parts A & B and stand-alone Part D during the study period
- Three study drugs were examined (Table 1): acarbose tablet, calcitonin salmon nasal spray (NS), and venlafaxine extended release (ER) tablet*
- Control drugs were identified to compare study drugs to those approved via traditional bioequivalence studies
- Control drug criteria: same indication, 1st generic was approved during study period
- All drugs were identified using National Drug Codes (NDC) in the Part D data and were identified as brand/generic using FDA application numbers and NDC numbers from First Databank and FDA drug dictionaries
- Outcomes of interest:
  - Switch from brand drug to generic drug
  - Switchback from generic drug to brand drug
- Trends in drug utilization were assessed using monthly prescription fills (Figure 1)
- EventFlow software was used to qualitatively visualize drug use patterns (Figure 2)
  - Index date: Date of approval of the first generic product
  - EventFlow (www.cs.umd.edu/hcil/eventflow) is a research prototype developed at the Human-Computer Interaction Lab of the University of Maryland College Park

Table 1. Study drugs

Study Drug	1st Generic Approval Date	BE study design	Control Drug(s)	1st Generic Approval Date
Acarbose (Precose®)	May 2008	*in vitro* studies alone if Q1/Q2 the same	Nateglinide (Starlix®)	Sep 2009
Calcitonin salmon NS (Miacalcin®)	Nov 2008	active polypeptide ingredient sameness, comparable immunogenicity; no *in vivo* studies necessary if Q1/Q2 the same	Alendronate (Fosamax®)	Feb 2008
Venlafaxine ER tablet*	Jun 2010 (capsule) Aug 2010 (tablet)	*in vivo* BE fed studies only; fasting studies not recommended	Bupropion ER (Wellbutrin XL®) Paroxetine ER (Paxil CR®) Sertraline (Zoloft®)	Dec 2006 Jun 2007 Aug 2006

*Venlafaxine generics were approved after the currently available data so are not presented in this poster; analyses involving venlafaxine are in progress with additional years of data (2010, 2011)

Results: utilization and switching patterns for acarbose and calcitonin salmon nasal spray

Figure 1. Monthly drug utilization

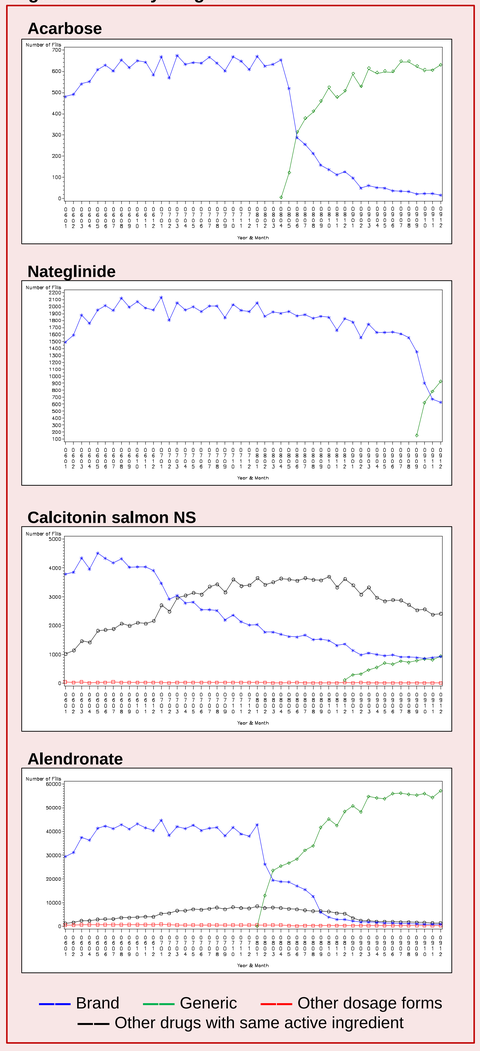
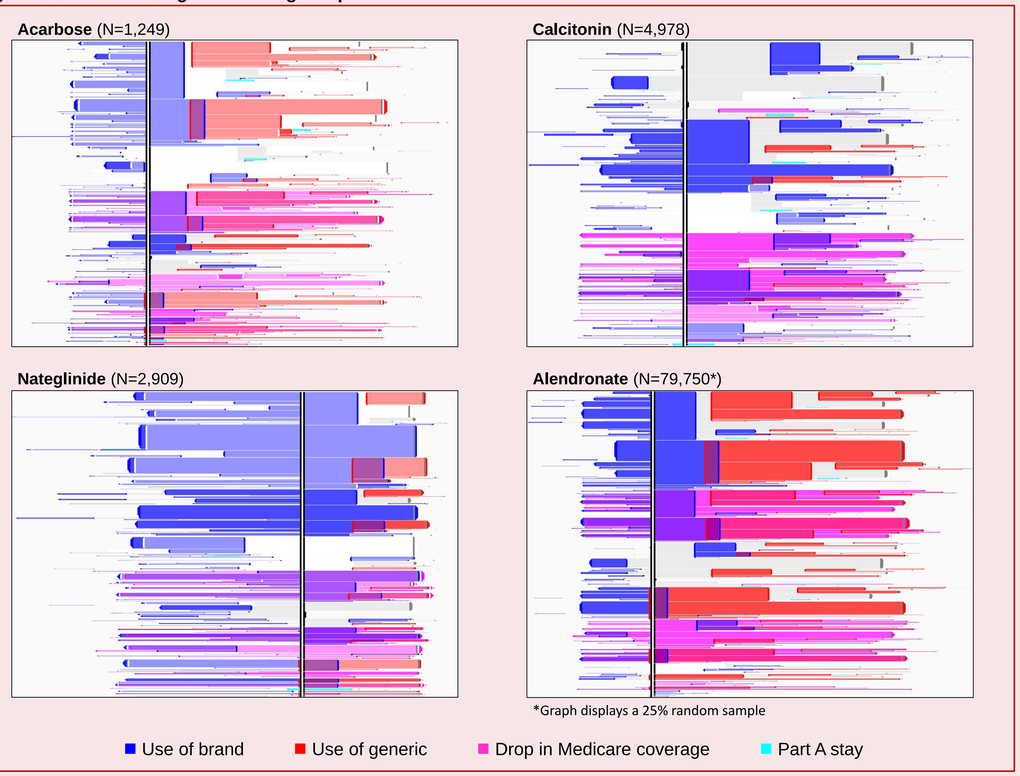


Figure 2. EventFlow diagrams of drug use patterns



- Acarbose
  - First year generic availability decreased brand utilization by 59%
  - Monthly generic utilization reached pre-generic brand levels within 18 months
  - A large proportion of those on brand acarbose switched to generic during the study period
  - A lower proportion appear switch from brand to generic control drug nateglinide, which may partially be due to the shorter follow-up period
- Calcitonin salmon NS
  - First year generic availability decreased brand utilization by 38%
  - Generic and brand drug use were approximately equal at 12 months post-generic availability
  - A small proportion of those on brand calcitonin switched to its generic during the study period
  - A large proportion of those on brand control drug alendronate switch to its generic within the first six months of generic availability

Conclusions

- Utilization and generic uptake varies between drugs, but there is minimal switchback from generic to brand among studied drugs
- Assessing generic drug utilization and switching patterns using administrative data is complex and needs to take into account a number of factors including the number of generics on the market, other dosage forms (e.g. calcitonin salmon as NS or injection), availability of other drugs in the class, and patent litigation
- Findings will have significant clinical and policy impact on current and future drug use, and will inform the FDA on strategies for monitoring the post-approval drug safety, effectiveness, usage, and substitution patterns of generic drugs

Supplemental work

- Ongoing work with administrative claims:
  - Addition of data (2010, 2011) to continue examining generic drug use, switching from brand to generic, and switching back from generic to brand
  - Investigation of medical service utilization associated with generic switching
- Systematic literature review of published clinical trials and observational studies on outcomes of brand and/or generic drug use for 3 study drugs
- Surveys of patients' and physicians' experience about brand and generic drug use to determine if controversy around generic drug approval has impacted perceptions of generic drugs

Disclaimer: The views expressed in this presentation are those of the presenters and should not be interpreted as those of the FDA.