Comparison of generic-to-brand switchback patterns for generic and authorized generic drugs

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Background

- Generic drugs play an important cost-saving role in the U.S. healthcare system. But, not all patients and providers are willing to use generic drugs. Patients' or physicians' personal opinions about generic drugs may affect their acceptance, and this can indirectly affect the perceived safety and efficacy of generic drugs.
- Generic drugs can enter the U.S. market via two mechanisms:
  1. Generic drugs (i.e., "generics") may be approved by the U.S. Food and Drug Administration (FDA) via an Abbreviated New Drug Application (ANDA) which requires demonstration of bioequivalence;
  2. Authorized generics (AGs) can enter the market under the reference products New Drug Application (NDA), and are pharmaceutically and therapeutically identical to the brand product.
- Comparing the utilization patterns of generic and authorized generic drugs provides a proxy for brand vs generic comparison.

Objectives

- To determine if there is post-marketing evidence to support potential differences between brands and generics by using a proxy comparison of generic-to-brand and AG-to-brand switchback rates, which minimizes potential selection and perception biases.
- Switchback was defined as a patient switching from the AG or generic product back to the branded drug.

Methods

- A series of retrospective cohort studies were conducted using administrative claims and electronic medical record (EMR) data (1999-2014).
- Eligible patients first received select branded drugs and then were switched to an AG or generic within 30 months of generic entry.
- Brand-to-AG and brand-to-generic switchers were followed for up to 30 months from the index switch date to evaluate brand switchbacks.
- Multivariable Cox proportional hazards models were used to evaluate factors associated with the time to switchback, reporting the median estimated hazard ratio (HR) and 95% confidence interval (CI) across 1000 bootstrapped samples.
- Switchback rates were compared over time between patients on AGs versus generics using Kaplan-Meier curves.
- Because of market fluctuations in AG and generic availability, follow-up time was censored at the earliest time when we stopped observing claims for either the AG or all existing generics.

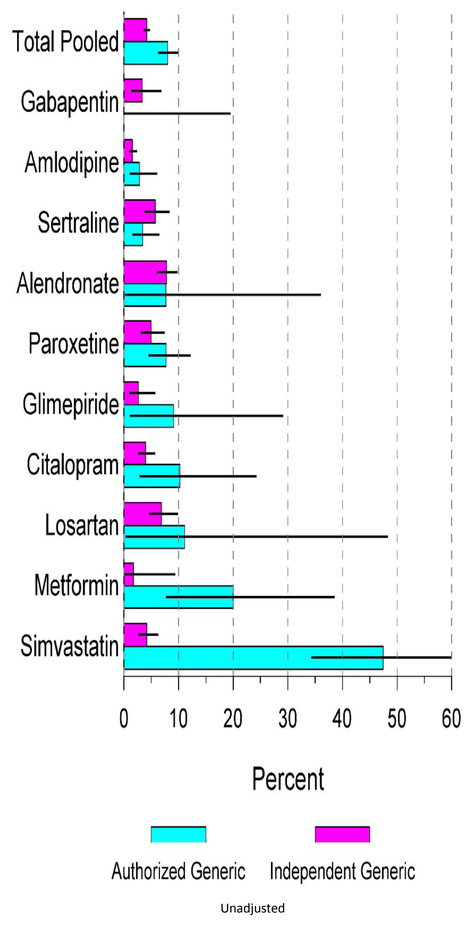
Drug	First Brand (date)	First AG (date)	First generic (date)
Alendronate	9/29/95	2/6/08	8/4/08
Amlodipine	7/31/92	3/23/07	3/23/07
Citalopram	7/17/98	10/28/04	10/28/04
Gabapentin	12/30/93	10/8/04	10/4/04
Glimepiride	11/30/95	9/30/05	10/6/05

Drug	First Brand (date)	First AG (date)	First generic (date)
Losartan	4/14/95	4/6/10	4/6/10
Metformin ER	10/13/00	10/10/03	10/28/03
Paroxetine	12/29/92	3/5/03	9/8/03
Sertraline	12/30/91	8/14/06	8/14/06
Simvastatin	12/23/91	6/23/06	6/23/06

Results

- In the full cohort, the first person-drug combination was selected and subsequent observations for other drugs were excluded. This resulted in 5542 unique patients in the full cohort, but 5929 unique person-drug combinations (867 on authorized generic and 5062 on generics).
- In the unadjusted cohort, 264 patients (4.8%) switched back to brand, including 67 (8.0%) in the AG group and 197 (4.2%) in the generic group.
- In multivariable models, the rates of generic-to-brand and AG-to-brand switchback were similar (HR=0.86; 95% CI 0.65-1.15).
- The likelihood of switchback was higher for alendronate and simvastatin and lower for amlodipine compared with other drugs in the cohort.
- Overall usage patterns were more volatile for AGs, with 50% of AG users switching to a different product (brand or generic) within 12 months.

Percentage of Switchbacks



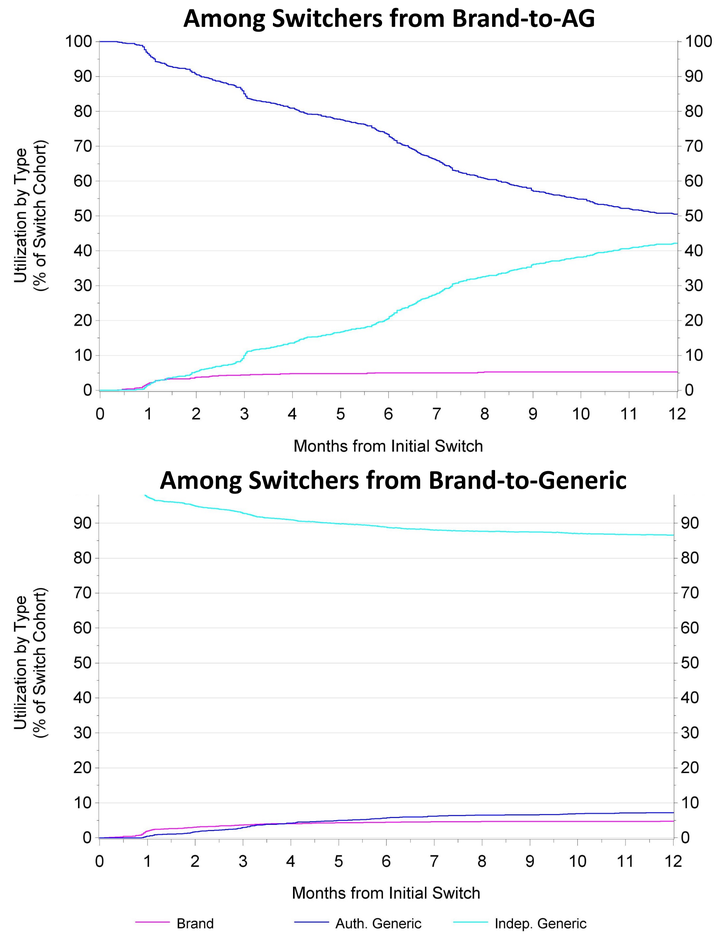
Unadjusted

Multivariable Switchback Models (1000 bootstraps)

	Hazard Ratio	95% Confidence Interval
Generic (reference = authorized generic)	0.86	0.65-1.15
Age	1.02*	1.01-1.02
Male	0.59*	0.44-0.80
Proportion of pre-index brand medication use	2.43*	1.45-4.07
Defined daily dose prior to switching	0.85	0.72-1.01
Charlson comorbidity index	1.02	0.90-1.16
Pre-index hospitalization	0.87	0.52-1.48
Pre-index ED visit	1.02	0.67-1.56
Count of pre-index outpatient visits	1.02	1.00-1.02
Drug		
Alendronate	1.64*	1.20-2.23
Amlodipine	0.27*	0.17-0.42
Citalopram	1.16	0.79-1.70
Gabapentin	0.74	0.34-1.62
Glimepiride	0.68	0.31-1.46
Losartan	1.29	0.80-2.10
Metformin XR	1.03	0.46-2.30
Paroxetine	1.09	0.74-1.60
Sertraline	1.08	0.71-1.62
Simvastatin	1.81*	1.30-2.54

The eligible sample includes all people that switched from brand to a generic or authorized generic. A series of regression models, each with an indicator for one drug, compared each specific drug with all other drugs combined. * P<0.05

Time to Next Change After Initial Generic Switch



Discussion

- Similar likelihood of generic-to-brand switchbacks between AG and generic users (P>0.05).
- Evidence is not sufficient to indicate that differences between ANDA-approved products (our generic group) and the reference listed drug (our AG group) are driving generic-brand switchbacks.

Conclusions

- Results show a similar likelihood of switchback between AGs and generics, indirectly suggesting equivalent efficacy and tolerability between generic and branded drugs.
- Reasons for differences in switchback rates among specific products need to be further explored.

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