Switching Patterns of Mixed Amphetamine Salt Products Among Patients in the Sentinel Distributed Database

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BACKGROUND

Adderall (dextroamphetamine sulfate, dextroamphetamine saccharate, d,l-amphetamine aspartate monohydrate, and amphetamine sulfate) is a central nervous system stimulant indicated for the treatment of **attention deficit hyperactivity disorder** (ADHD) and **narcolepsy**.

The immediate-release brand product Adderall was discontinued in 2010. Generic equivalents are widely used in the form of mixed amphetamine salt (MAS) products. The current reference standard is a generic equivalent manufactured by Barr Pharmaceuticals, Inc. (subsidiary of Teva) abbreviated new drug application (ANDA) 040422. These generic MAS products, particularly the immediate release tablet products of **Aurolife Pharma, LLC (ANDA 202424)**, have been the subject of spontaneous reports to the Drug Quality Reporting System, a subset of FDA's MedWatch. Most complaints described lack of effectiveness and a need for a dose increase after switching to Aurolife MAS products from other MAS products.

Patients may switch to a therapeutically equivalent generic, another formulation, or another drug due to poor drug effectiveness, adverse events, or changes in pharmacy availability or cost.

OBJECTIVE

To examine utilization and switching patterns among individuals with ADHD or narcolepsy treated with MAS immediate release products in the FDA Sentinel Distributed Database (SDD).

METHODS

We identified ADHD or narcolepsy patients (age 15-64 years) with prevalent use (for utilization analyses) and at least a 60-day continuous supply (for switching analyses) of a single dose and product of a generic MAS immediate release medication grouped by ANDA codes associated with specific manufacturers (Table 1). Analyses were conducted among five Sentinel Data Partners with a query period from January 1, 2013 through December 31, 2019. These five Data Partners are a subset of the SDD and do not include patients with Medicare coverage. Eligible MAS immediate release users were required to have 183 days of health plan enrollment prior to the index dispensing, with allowable gaps in coverage of up to 45 days.

We identified the exposures of interest, MAS products in different ANDA groups, using National Drug Codes (NDCs). All qualifying treatment episodes were included; cohort re-entry was allowed.

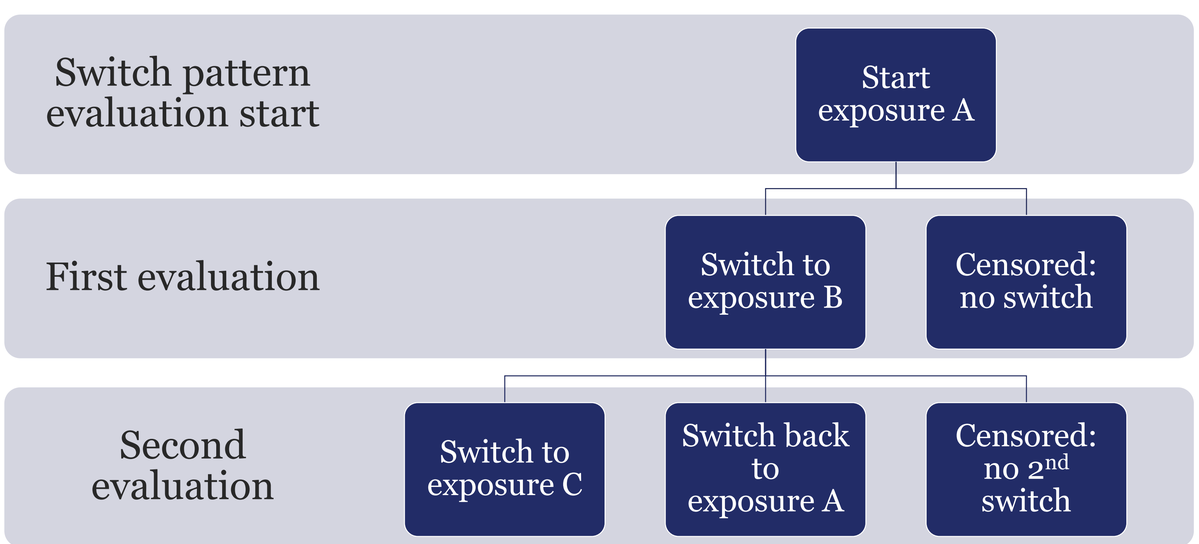
Table 1. Manufacturers and ANDA products of interest

Manufacturer	ANDA Number
Aurolife Pharma, LLC	202424
SpecGX LLC, a subsidiary of Mallinckrodt	040440
Barr Pharmaceuticals Inc., a subsidiary of Teva	040422
Sandoz, a Novartis division	040439
NorthstarRx LLC Pharmaceuticals	040480

We first described product utilization for each of the MAS products of interest and other MAS products excluding those of interest. Then we evaluated several switch patterns over two switch evaluation periods among those prevalent users considered stabilized on the product and dose of interest (at least 60-day continuous supply):

1) to a higher dose of any MAS immediate release product,
2) away from an ANDA product of interest, and
3) to an ANDA product of interest, either the same or another MAS immediate release product.

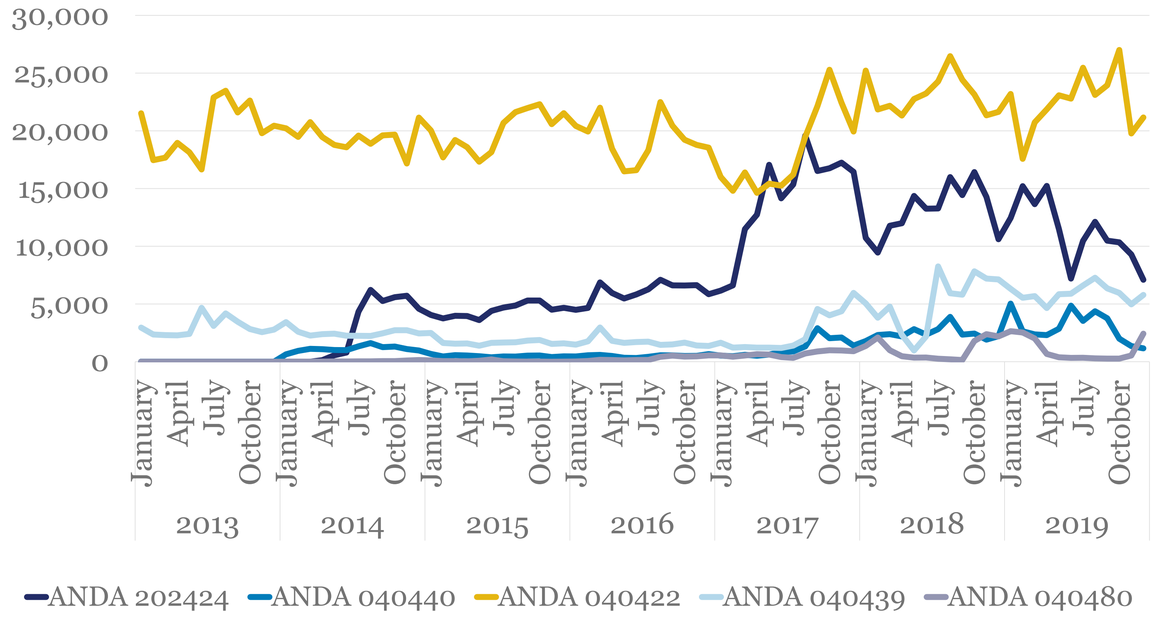
Figure 1. Potential switch patterns



RESULTS

Over the study period, we observed the greatest utilization for ANDA 040422 products (525,771 episodes; 290,760 patients), followed by ANDA 202424 (181,693 episodes; 114,219 patients) and ANDA 040439 (62,363 episodes; 44,450 patients).

Figure 2. MAS users over time

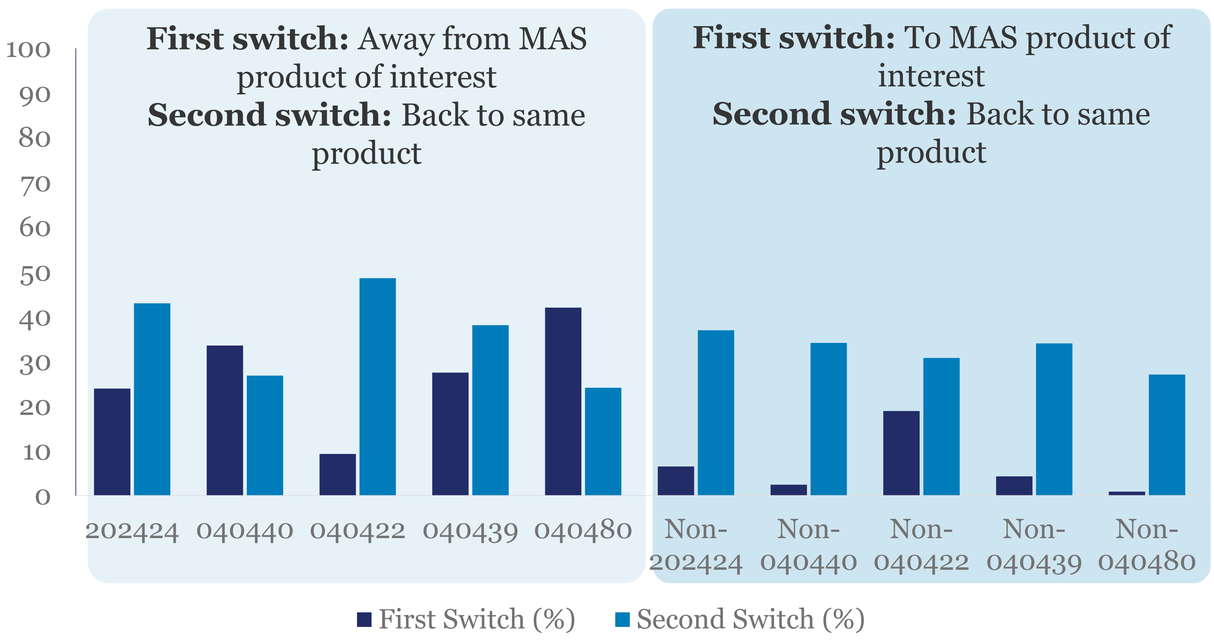


Few episodes of any of the five ANDA cohorts of interest resulted in a switch to a higher dose product (range 1-3%).

The proportion of episodes resulting in a switch to another product varied by ANDA group: 42.0% of 040480 episodes resulted in a switch to another product, contrasted with only 9.3% of 040422 episodes. Of those with a first switch, ANDA 040422 episodes were most likely (48.6%) to end with a switch back to the same product and ANDA 040480 episodes were least likely (24.1%).

Of those episodes that switched to an ANDA product of interest after starting on another MAS product, about half (range 46.4% to 58.3%) switched back to the first product. These switches had a median time to switch of about 30 days.

Figure 3. Proportion of episodes with a switch



CONCLUSIONS

- Generic MAS immediate release products are used heavily.
- Few patients increase dose after 60-days of stable use.
- Of those that switch to an ANDA product of interest, about half switch back to their prior product after a month, regardless of which ANDA they started on. A large proportion of those using ANDA 040480 products switch to a new product without switching back, while a large proportion of those using ANDA 040422 switch back to the same product. These patterns appear to correlate with the number of dispensings for the period.
- Results from these analyses, which did not consider factors such as market availability, pharmacy selection of generic(s) to stock, and patient and/or provider preferences, did not support the reports of decreased effectiveness for any selected ANDA product based on the switching patterns observed.

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- The views expressed in this presentation represent those of the presenters and do not necessarily represent the official views of the U.S. FDA.