# PATTERN OF USE AND SAFETY PROFILE OF BRANDED VS GENERIC ANTIEPILEPTIC DRUGS

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**Introduction:** Epilepsy is a neurologic disorder that affects around 50 million people world-wide, with a significant higher prevalence in developed countries. AntiEpileptic Drugs (AEDs) are generally considered non-expensive medications; nevertheless, given their high prevalence of use, they largely contribute to the expenses of the National Healthcare System. Concerns on safety, adherence and economic impact of AEDs have driven scientific attention to generic AEDs.
In this study, we aimed at assessing the risk of generic compared to branded AEDs in terms of occurrence of Adverse Drug Reactions (ADRs) leading to hospitalizations and/or emergency access to Emergency Department (ED).

**Material and methods:** Study Design and data source: We conducted a population-based cohort study of new-users of AEDs using administrative databases of the Italian region of Tuscany, that include information on prescriptions of drugs for outpatient use, hospital admissions, admissions to emergency care, exemptions from copayment, and causes of death. Inclusion and exclusion criteria: We included all subjects with at least one prescription of any AEDs (ATC: N03*) between the 1st of January 2015and the 31st of December 2015and with at least 365days of look-back. We excluded subjects that in the look-back period had at least one AED prescription or prescription of antineoplastic drugs (ATC: L01*) and/or hospitalization related to neoplasia. Exposure variable: The AEDs index prescription was classified in four mutually exclusive categories: i) available only as branded; ii) branded with generic available (B); iii) generic (G); iv) composed of two or more different active principles. Patients were classified as switchers if swapped from B to G or viceversa. In the comparative safety analysis, we considered only categories ii) and iii). Outcomes: Outcomes were hospitalizations and/or access to ED for any reasons (all-cause events) and for AEDs related adverse drug reactions (drug-reaction events). Follow-up: For each subject, we considered the first AED prescription as the index prescription, and its prescription date as the index date. Follow-up began at index date and continued until outcome, death, exit from database, end of coverage, switch from G to B or viceversa, switch of active principle, prescription and/or hospitalization related to neoplasia or 365days after index date, whichever came first. Statistical analysis: Subjects with a generic AED first prescription (G) were matched to 4subjects with a branded AED first prescription (B), using the propensity score nearest neighbour matching method, based on the following matching variables: gender, age, indication of use, comorbidities, income. We applied Cox regression models to estimate Hazard Ratios (HRs) of all-cause events or drug-reaction events for G versus B.

**Results:** We identified 32867AED new-users, including 2141(6.5%) users of branded AEDs without generics available, 24580 (74.8%) users of branded AEDs with generics available (B), 5790 (17.6%) users of generic AEDs (G), and 356(1.1%) users of two or more concomitant AEDs. There were 1458(5.9%) switchers from B to G and 839(14.5%) from G to B; 514(35.3%) back switchers to B and 211(25.1%) to G. After the propensity score matching, the cohort included 5605G new-users and 21167B new-users. The subjects with all-causes events were 1994(35.6%) and 7938(37.5%) among G and B new-users, respectively; those with drug-reactions events were 757(13.5%) and 3008(14.2%) among G and B new-users, respectively. The comparative safety analysis did not show any association between the risk of event and use of G or B.

**Conclusions:** In 2015generic AEDs were under-used in Tuscany compared to branded; although the proportion of patients switching from generic AEDs to branded AEDs was not low, many switched back to generics. The study confirmed that the generic AEDs are as safe as the branded ones.