

# Antiepileptic Drugs: prescribing pattern and potential drug-drug interaction risk in general practice

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**Background:** In the last years, increasingly prescriptions of antiepileptic drugs (AEDs) were observed in general practice, particularly for indications other than epileptic disorders. Gabapentin and Pregabalin are mainly involved in this growing trend of AEDs use. As a consequence, since 2007, the Italian National Health System (NHS) introduced a health-policy intervention, which restricted the refundability of newer AEDs pregabalin and gabapentin in diseases for which strong scientific evidence has been provided. Moreover, most of AEDs are also involved in potential clinically relevant drug-drug interactions.

**Objectives:** To analyze the prescribing pattern of newer and older AEDs; to assess the exposure to potential drug-AED interactions in a general practice setting of Southern Italy.

**Patients and Methods:** We analysed a population of almost 150.000 individuals living in Caserta and registered in the lists of 123 general practitioners (GPs). Patients who received at least one AED prescription during 2005-2011 were identified. We calculated the one-year prevalence and incidence of AED use by drug class and single ingredient over the study period; AEDs consumption was evaluated as defined daily dose (DDD)/100000 inhabitants/day. Potentially clinically relevant drug-AED interactions were identified according to Drug Interaction Facts. Drugs potentially interacting were evaluated as exposition overlapping days between AEDs and potentially interacting drugs.

**Results:** Prevalence of older AED use slightly increased from 10.7/1,000 inhabitants (10.1-11.2) in 2005 to 13.0/1,000 inh. (12.4-13.6) in 2011, while a strong increase of newer AED use was observed from 14.7/1000 inh. (14.1-15.3) to 22.3/1000 inh. (21.5-23.0) until 2006, followed by a strong decrease to 16.2/1000 inh. (15.6-16.9) in 2011. Among older AEDs, phenobarbital and valproate were the most widely used in 2011, accounting for 21.2% (21.1-21.3) and 16.2% (16.1-16.3) of total AED consumption (DDD 163.7/100000 inh./day and 125.2/100000 inh./day), respectively. Among newer AEDs, oxcarbazepine accounting for 10.9% (10.8-11) with a consumption of 84.1/100000 inh./day DDD and lamotrigine, 10.8% (10.7-10.9) with a consumption of 83.2/100000 inh./day DDD were the most prescribed molecules during 2011. However pregabalin 45.4/10000 inh./day (41.9-48.9) and gabapentin 10.0/10000 inh./day (8.4-11.6) incidence of use remain the highest among newer AEDs users during 2011. The main indication of use was epileptic disorders for older AEDs and neuropathic pain for newer AEDs. A high number of patients treated with older AEDs, in particular primidone (66,9 day/year person), carbamazepine (30,7 day/year person), phenytoin (29,3 day/year person), phenobarbital (28,3 day/year person) and valproic acid (27,8 day/year person), received co-prescription at at risk of clinically relevant interaction. Among newer AEDs, topiramate showed the highest risk of possible DDIs (1,9 day/year person). Acetylsalicylic acid (3,6 day/year person), nifedipine (2,7 day/year person) dexamethasone (1,4 day/year person) and warfarin (1,1 day/year person) were the most frequently co-prescribed drugs which may interact with AEDs.

**Conclusion:** Older AEDs were mainly used in the treatment of epileptic disorders, while newer compounds were also preferred for conditions other than epilepsy, in particular neuropathic pain. The strong decrease of newer AEDs use during 2007 could be explained with the last health regulatory measures that revised re-imburement criteria for gabapentin and pregabalin. In AEDs users, a relevant exposition to potentially harmful DDIs was shown. The co-prescription should be evaluated with caution or avoided, if possible. Whenever possible, pharmacological options, which do not interact with AEDs, should be prescribed to AED users.