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Re: Pregabalin prescriptions in the United Kingdom – a drug utilisation study of The Health Improvement Network (THIN) primary care database by Asomaning et al.

To the Editor:

We have read with great interest the recent study on the use of pregabalin, that was reported in the International Journal of Clinical Practice by Asomaning et al., representing Pfizer, the original Marketing Authorization Holder for pregabalin (1). We, that is, the authors of this letter, have authored three original papers (2,3) (one yet to be published) and a review on the same topic (4). While we appreciate this contribution to a difficult and somewhat controversial subject, we have some concerns regarding the relevance of the data source utilised in their study and consequently the conclusions reached by the authors.

We wish to draw attention to two potential issues, both related to the choice of data sources: (i) the use of *prescribed* dose of *single* prescriptions compared with *dispensed* dose for the *full pattern of dispensings* for each individual and (ii) the sampling of patients from a general practice database that does not hold data on secondary and tertiary care. Both issues will infer a bias towards the null in estimates of the proportion of patients using pregabalin above licensed dosages.

The prescribed dose may not accurately reflect an individual's drug use, as prescribed drugs may not be dispensed at all, or may be dispensed in a manner that deviates from the intent of the prescriber (referred to as primary non-adherence) (5,6). The distinction between prescribed and dispensed drug is of particular importance when considering drugs suspected of carrying a misuse potential, where substance-seeking behaviour might involve multiple prescribers (7). Thus, while the daily prescribed dose for the single prescription may be within the recommended clinical range, the total dispensed dose may be substantially higher when taking into account the individual's total dispensing pattern, as demonstrated in previous studies (2,3).

In Europe, pregabalin is indicated for the treatment of epilepsy, neuropathic pain and generalised anxiety disorder (8). Many patients thus receive pregabalin treatment as part of secondary and tertiary care (9,10). In the previous studies (2,3), use of pregabalin in doses exceeding the approved level was shown to be associated with a history of epilepsy, a history of substance use disorder, previous use of opioid analgesics and other factors which are expected to be less prevalent in primary care. Consequently, the restriction to primary care prescribing, will likely result in estimations of pregabalin use above licensed doses that do not reflect actual use.

Asomaning et al. only considered prescribed doses of single prescriptions, as opposed to taking the full dispensing pattern of each patient into account (1). As a result, they found that pregabalin is prescribed in doses exceeding the licensed daily dose of 600 mg in only 1.0% of patients (1), which is markedly lower than the previous studies reporting proportions of 8.5% (2) and 9.6% (3). While Asomaning et al. notes that 'the reasons for this difference are unknown' (1), we believe that the two explanations mentioned above likely explain this discrepancy.

Postmarketing surveillance of drug safety and drug utilisation is of great importance. As the choice of data sources is imperative to the external validity of such studies, data sources must be chosen meticulously and with attention to possible pitfalls. In this case, we do not believe that the researchers have sufficiently accounted for such, and consequently we do not believe that the results from their study reflect the true picture of pregabalin utilisation. While we acknowledge that the results complement the existing literature which did not take prescribed regimens or use in the UK into account, the abuse potential of pregabalin, particularly among individuals with substance use disorder, must still be considered unresolved.

Disclosure

None.

A. Pottegård,[1] M. Tjäderborn,[2] O. Schjerning[3,4] J. Nielsen,[3,4] P. Damkier,[1,5] R. Bodén,[6,7]

[1]Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, Odense, Denmark
[2]Clinical Pharmacology, Department of Drug Research, Linköping University, Linköping, Sweden
[3]Psychiatry, Aalborg University Hospital, Aalborg, Denmark
[4]Department of Clinical Medicine, Aalborg, University, Aalborg, Denmark
[5]Department of Clinical Chemistry and Pharmacology, Odense University Hospital, Odense, Denmark
[6]Psychiatry, Department of Neuroscience, Uppsala University, Uppsala, Sweden
[7]Department of Medicine Solna, Centre for Pharmacoepidemiology, Karolinska Institutet, Stockholm, Sweden
E-mail: apottegaard@health.sdu.dk

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