Older Antiepileptics and Polytherapy Are Linked to an Increase in Adverse Effects

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

MADRID — Adverse events are more common in patients who take older antiepileptic drugs or who take more than one antiepileptic, compared with patients on monotherapy or newer agents.

"The adverse effect profiles of antiepileptic drugs are often determining factors in drug selection, and yet adverse effects may be overlooked in everyday clinical practice," Joyce A. Cramer wrote in a poster presented at the annual congress of the European Federation of Neurological Societies.

Ms. Cramer, a research scientist at Yale University, New Haven, Conn., conducted a population surveillance study to evaluate the adverse effects of both newer and older antiepileptic drugs (AEDs). The cross-sectional study was conducted in six European countries and consisted of a single clinical examination and structured interview.

The study population comprised 1,019 patients (mean age, 31 years) who had been on a stable dosing regimen for a median of 13 months. Of those, 57% were on monotherapy, and 43% were on polytherapy.

Most of the patients (71%) were taking at least one older AED (carbamazepine, clobazam, clonazepam, phenobarbital, phenytoin, or valproate). The rest were taking at least one newer AED (gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, tiagabine, topiramate, and zonisamide).

At least one adverse effect occurred in 68% of the patients. Newer AEDs were associated with fewer reports of adverse effects than were older drugs (61%, compared with 71%, respectively), and monotherapy was associated with fewer reports of adverse effects than was polytherapy (66%, compared with 71%).

Neurologic adverse effects were more common in those taking older AEDs than in those taking newer AEDs (60% vs. 54%, respectively), as were systemic adverse effects (42%, compared with 33%).

Neurologic adverse effects were also more common in patients on polytherapy than in those on monotherapy (64% vs. 53%), although the percentage of patients reporting systemic adverse effects was equal in these two groups (40%).

Adverse effects that were significantly more common in those taking the older drugs, compared with the newer drugs, were cognitive slowing (30% vs. 22%), sedation (30% vs. 23%), and tremor (18% vs. 10%).

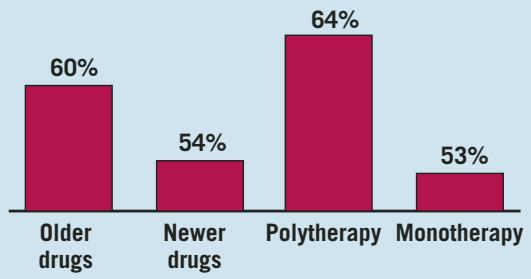
Adverse effects that were significantly more common in those taking polytherapy, compared with monotherapy, were cognitive slowing (36% vs. 22%), psychological problems (31% vs. 22%), tremor (21% vs. 11%), and gait disturbances (12% vs. 7%).

A logistic regression analysis concluded that patients on newer AEDs were 36% less likely than were those on the older drugs to report at least one adverse effect. Treatment modifications were 52% more likely in those reporting adverse effects; at the study visit, 23% of patients changed therapy, mostly because of an adverse effect.

Ms. Cramer noted that patients who were taking levetiracetam were 67% less likely to report an adverse effect than were those who were not taking the drug, and those taking lamotrigine were 49% less likely to report an adverse effect than were those not taking lamotrigine.

The study was sponsored by UCB Pharma Inc., the company that manufactures levetiracetam. Ms. Cramer is a consultant for the company. ■

Neurologic Adverse Events With Antiepileptic Drugs

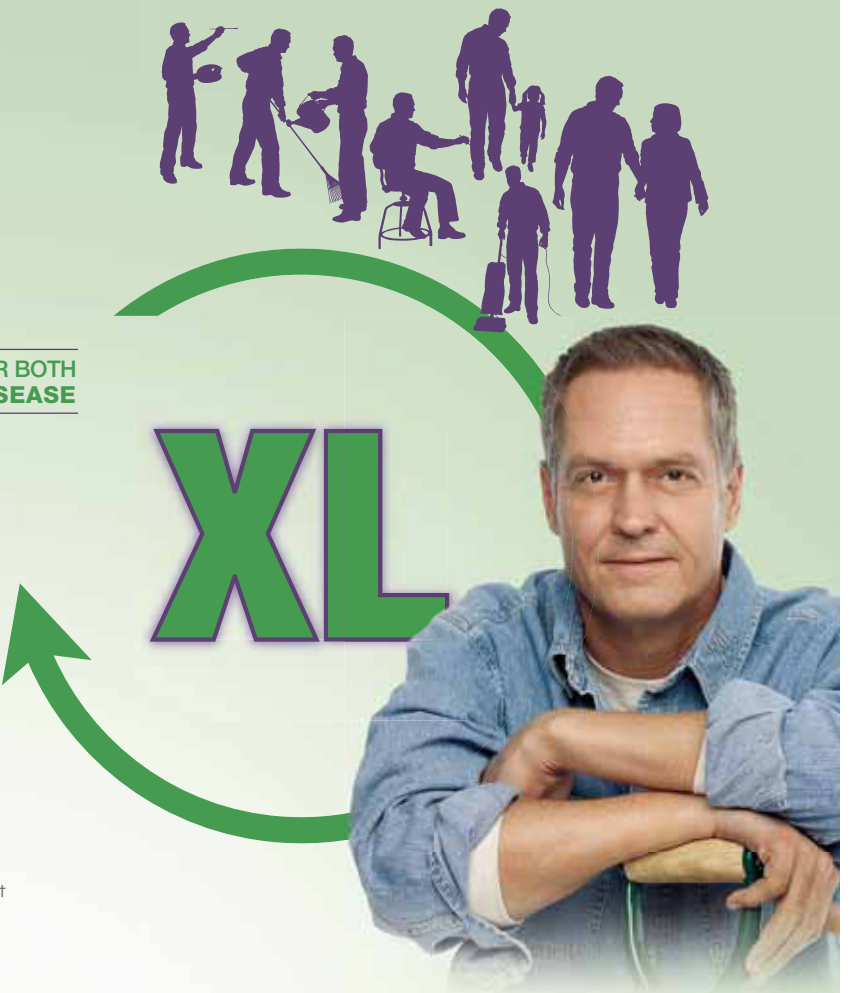


Note: Percentage data based on a study of 1,019 patients dosed for a median of 13 months.
Source: Ms. Cramer

ELSEVIER GLOBAL MEDICAL NEWS

INTRODUCING
REQUIP XL
THE ONCE-DAILY ORAL DOPAMINE AGONIST FOR BOTH EARLY AND ADVANCED PARKINSON'S DISEASE

Once daily for more time in motion



- One daily dose for smooth delivery[1]
- Simple conversion, simple titration
- Reduced "off" time by more than 2 hours, relative to baseline, when added to L-dopa[2*†]

Important Safety Information

REQUIP XL has been associated with sedating effects, including somnolence, and the possibility of falling asleep while engaged in activities of daily living, including operation of a motor vehicle. REQUIP XL should be discontinued if these events occur; it is unknown if dose reduction will eliminate episodes of somnolence. Prescribers should reassess patients for somnolence throughout treatment.

Syncope or symptomatic hypotension may occur, particularly during initial treatment or dose titration. Patients should be cautioned against rising rapidly after sitting or lying down. Elevation of blood pressure and changes in heart rate may also occur.

Because of possible additive effects, caution should be exercised with patients who have sleep disorders or are taking sedating medications, alcohol, CNS depressants, or medications that increase ropinirole plasma levels.

Hallucinations may occur at any time during treatment. REQUIP XL may potentiate the dopaminergic side effects of L-dopa and may cause and/or exacerbate pre-existing dyskinesias.

Patients should be informed that impulse control symptoms, including compulsive behaviors such as pathological gambling and hypersexuality, have been reported in patients treated with dopaminergic agents, including ropinirole. Although it is not proven that the medications caused these events, these urges were reported to have stopped in some cases when the dose was reduced or the medication was stopped.

Some epidemiologic studies have shown that patients with Parkinson's disease have a higher risk (perhaps 2- to 4-fold higher) of developing melanoma than the general population. Whether the observed increased risk was due to Parkinson's disease or other factors, such as drugs used to treat Parkinson's disease, was unclear.

Although REQUIP XL has not been associated with an increased risk of melanoma specifically, its potential role as a risk factor has not been systematically studied. Patients using REQUIP XL should be made aware of these results and should undergo periodic dermatologic screening.

*A 6-month, randomized, double-blind, placebo-controlled study of 391 patients with Parkinson's disease who were not optimally controlled with L-dopa. As adjunctive therapy to L-dopa, patients were randomized to either REQUIP XL + L-dopa or placebo + L-dopa. The primary end point was mean change from baseline in hours "off" at week 24.
†Relative difference to placebo was 1.7 hours.

For more information about REQUIP XL, visit **www.requipxl.com**.
Please see Brief Summary of Complete Prescribing Information on the next page.

GlaxoSmithKline

REQUIP® XL™ (ropinirole extended-release tablets)