

Letters

Is Prozac more effective than generic fluoxetine?

Upon its introduction in 1987, fluoxetine revolutionized drug therapy for mood disorders and has become a cornerstone in depression treatment. After 14 years of being the sole manufacturer of fluoxetine (under the brand name Prozac), Eli Lilly and Company's exclusivity patent expired.¹ Generic fluoxetine is now available through multiple manufacturers.

While use of generic fluoxetine rather than Prozac will decrease medication costs, the question arises: Is the brand-name drug more effective than its generic equivalent? Some anecdotal reports have suggested a clinical difference, but these claims have not yet been supported in the literature.

Some clinicians have found that select patients require a higher dosage of generic fluoxetine than Prozac to control their symptoms, but several issues may contribute to these increased requirements. First, depression and depressive symptoms wax and wane; an increase in symptoms may be part of the course of illness rather than differences between brand and generic formulations.

Increased symptoms may also reflect patient bias. The patient knows he or she is taking a generic and may be more inclined to notice or report symptoms. Additionally, some patients who believe generics are less effective than brand-name equivalents experience a reverse placebo effect—their belief that a generic drug is inferior diminishes its effectiveness. Finally, subtle differences in bioavailability and bioequivalence between the brand-name and generic drugs may be seen clinically.

To receive FDA approval, a generic drug must be proven to be therapeutically equivalent to its brand-name counterpart. This entails both pharmaceutical equivalence (identical amounts of the same ingredient in the same dosage form and route of administration) and bio-equivalence (comparable rate and extent to which the active ingredient is absorbed and becomes available at the site of action).² Statistical analysis of pharmacokinetics includes evaluating measures such as area under the curve and peak concentration. The test drug and reference drug are compared by calculating the 90% confidence interval for their respective population geometric means. The calculated confidence interval should fall within the bioequivalence limit, typically between 80 and 125% for the population geometric mean. Other factors typically

considered include the logarithmic transformation of pharmacokinetic data, methods to evaluate sequence effects, and evaluation of outlier data.³

Comparator generic drugs must be rigorously tested before receiving FDA approval. One would hope that the variability that may exist between the brand and generic product does not significantly change patient response.

To date, more than 20 companies have received approval or tentative approval for almost 50 generic fluoxetine products. The approval package data (which includes bioequivalency data) for these agents are not yet available.⁴

Still, there is no evidence that generic fluoxetine is less effective than Prozac, despite increased attention from patients, clinicians, and pharmaceutical companies. The bottom line is that each patient needs individual treatment. If symptoms increase or worsen, then increase the dosage, which would be done in any case. If adverse effects increase, lower the dosage. If a true difference is suspected in a specific patient, it should be promptly reported to the FDA, which evaluates drugs after marketing by regularly assessing product quality and investigating and evaluating allegations of drug product inequivalence.⁵

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'Clinically valuable' information

Current Psychiatry is the only journal in which I read the entire article. The quality of writing is excellent. The information is clinically valuable.

I hope *Current Psychiatry* continues and prospers.

William Goldsmith, MD

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MAOIs and pizza: food for thought

I greatly appreciated the review by Jonathan Cole, MD, and J. Alexander Bodkin, MD, on the use of MAOIs (June, p. 40) but would like to offer the following comments.

It is unfortunate that these potentially life-saving medications are being utilized less and less. While the authors note that excessively inclusive dietary restrictions are one reason for the MAOI's disuse, they appear to further discourage its use by including pizza as a food to avoid. More recent experience and research^{1,2} have demonstrated that commercially available pizza, as well as pizza produced without aged cheeses, is safe for consumption while taking MAOIs. In fact, the authors of the dietary instructions included with the Cole-Bodkin article are the primary researchers who reported on this food's safety.²

Because pizza is such a popular food, it is important to not restrict patients' consumption of it unless medically necessary.

Additionally, while Drs. Cole and Bodkin note that MAOIs are used primarily in treatment-resistant patients, it might have been useful for them to include a section on MAOI augmentation strategies, as well as the possible usefulness of prescribing these medications at dosages above their usual ranges.³

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References

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NMHA: Bar executions of mentally ill defendants

The National Mental Health Association (NMHA) commends the recent U.S. Supreme Court ruling that executing people with mental retardation is unconstitutional and cruel.

The ruling is confined to people with mental retardation, generally defined as those having an IQ of 70 or lower; NMHA urges the Supreme Court to make the same ruling for defendants with mental illness.

NMHA believes that mental illness can influence an individual's mental state at the time he or she commits a crime, can affect how "voluntary" and reliable an individual's statements are, can compromise the defendant's competence to stand trial and to waive his or her rights, and may affect the defendant's knowledge of the criminal justice system.

We are not suggesting that people with mental illness be exempt from criminal sanctions. We just feel that their punishment should not include the death penalty, which, for this population, is cruel.

The court is on the mark in recognizing a growing national consensus against using the death penalty on certain populations who do not fully understand the crime they have committed or its consequences. Defendants who have a mental illness, like those who have mental retardation, should not be executed.

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President and CEO
National Mental Health Association

React!

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- Do you disagree with the practices recommended by authors in this issue of *Current Psychiatry*?
- Do you know of research that substantiates or raises questions with what an author says?
- Do you have a case history that can supplement a topic in our pages?

We welcome your comments. Send them to Senior Editor Pete Kelly, pete.kelly@dowdenhealth.com. We'll publish those that our Editorial Board deems appropriate. And you'll hear back soon.