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LETTER TO THE EDITOR Open Access

Comment on "An update on recently approved long-acting injectable second-generation antipsychotics: Knowns and unknowns regarding their use"

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Dear Editor:

We read with interest Dr. VandenBerg's Psychopharmacology Pearl article[1] in the October 2022 issue of *Mental Health Clinician* discussing recently approved long-acting injectable second-generation antipsychotics. We appreciate that Psychopharmacology Pearl articles reflect the views and practices of authors, substantiated with evidence-based data as well as professional opinion and experience. However, we noticed inaccuracies regarding aripiprazole lauroxil (AL; Aristada, Alkermes Inc, Waltham, MA) in the VandenBerg article and would like to offer corrections and clarifications.

The article states, "The difference in molecular weight drives much of the difference in dose between" aripiprazole monohydrate (AM) and AL. For AL, the prodrug formulation developed using the proprietary LinkeRx technology (Alkermes) allows for the slow dissolution of drug particles, and that dissolution rate, not molecular weight, is the primary driver of the controlled and sustained release of aripiprazole over the dosing interval.[2] Indeed, the initiation formulation of AL (Aristada Initio, Alkermes) allows considerably more rapid dissolution than the maintenance formulation although the 2 formulations have the same molecular weight.[3,4]

The article also states, "In pharmacokinetic studies, higher serum concentrations were achieved with AM versus all labeled AL dosing strategies."[1] We are not aware of any head-to-head studies supporting this statement—only indirect comparisons of AM versus AL can be made. Further, no single variable, such as peak plasma concentration, provides a full characterization of antipsychotic exposure, and understanding the shape of the concentration-time curve is critical. Average plasma concentrations over the dosing interval, together with peak-to-trough concentration ratio, are more clinically meaningful than peak concentration alone. Large fluctuations in plasma concentration may negatively affect clinical response and tolerability,[5] and average plasma concentration may be similar for a drug with little concentration variation over the dosing interval and one with a substantially greater range between maximum and minimum plasma concentration values. Peak-to-trough ratios of serum aripiprazole concentrations are smaller with AL than with AM.[2,6,7]

Finally, the article states, "…patients who require higher oral maintenance doses may require AL 1064 mg more frequently than the labeled every 8 weeks."[1] Rather, patients who require higher doses than AL 1064 mg every 2 months (daily oral aripiprazole equivalent of 15 mg) may be transitioned, according to product labeling, to AL 882 mg monthly, which is equivalent to a daily oral aripiprazole dose of 20 mg or higher.[3]

We offer the clarifications here to enhance readers' understanding of AL pharmacokinetics and dosing, consistent with labeling approved by the US Food and Drug Administration. We hope that this information will help clinicians provide high-quality care to patients treated with long-acting injectable antipsychotics.

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