What's new? Isomers, metabolites and prodrugs, oh my!

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The terms racemic mixtures, single isomers, prodrugs, active metabolites, extended-release mechanisms were once remembered as the topics of early pharmacy school curriculum. Now they are often the source of confusion for practitioners and, sometimes, big money for manufacturers. Since 2011, nearly ten percent of the top 100 medications by sales were "new and improved" versions of previously released products with 4-5% being revised psychotropics.[1] Since these "new" products are released as brand name agents under patent protection, they are often priced much higher than their predecessors. Clinical evidence is limited to approval trials – a handful of placebo-controlled and/or active-controlled efficacy studies. Rarely, if ever, are the new agents compared head-to-head with predecessor products. Clinicians are faced with marketing claims that, while true statements (e.g., "The starting dose is the proven effective dose"[2]), may not have data to support clinical impact (i.e., differences in response or remission rates). In a time of financial strain for the healthcare system as a whole, the high cost of these new agents can be a hard pill to swallow. Evaluation of clinical utility must include efficacy, safety and cost as with any new medication. As head-to-head trials are extremely rare with these "new" medications, evidence-based comparisons may be limited to pharmacokinetic and pharmacodynamic properties of products. It is also important to use clinical common sense to compare new agents to their predecessors.

Sometimes the "new" medications even have new versions that are released. For example, desvenlafaxine succinate extended release tablet was released in 2008 under the brand name Pristiq®. Patent exclusivity for this product expired in early 2013. As of October 2013, desvenlafaxine is available as the succinate salt (Pristiq®), desvenlafaxine base (both generic and Khadezla) and desvenlafaxine fumarate extended release tablets.[3-5] What is the difference between these products? Other than solubility and clinically insignificant differences in half-life, nothing appears to be different. Clinical data in the package inserts (PI) for the products are all based on the original desvenlafaxine succinate studies. As of December 11, 2013 enter desvenlafaxine fumarate into PubMed and not one clinical trial will appear. Try to directly compare pharmacokinetic parameters between products and few of the parameters will be readily available. In the case of Pristiq®, the time to maximum concentration and half-life were listed in the original package insert (PI) back in 2008, but are absent from the most recent 2013 PI.[6]

Attempting to compare all of the "new" products that have been released in recent years is a daunting task for sure. This issue will examine six of these new products, focusing on clinically relevant differences between new products and predecessors where data are available. Additionally, the approval process for antidepressants will be reviewed. A toolbox will provide direct comparisons of available pharmacokinetics, FDA approval information, and cost for selected psychotropic medications with revised products on the market.

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