Dexmethylphenidate
A Viewpoint by Julie M. Zito

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In the past 2 years, the development, marketing and promotion of new stimulants have grown very active and are aimed at providing more convenient products (e.g. longer-acting products requiring fewer doses per day) or newer, possibly better products. Among these agents is dexmethylphenidate, the *d-threo*-enantiomer of racemic methylphenidate. To assess the potential role for the newly approved, patent-protected dexmethylphenidate requires attention so as to try to separate reasonable scientific inferences from personal/professional preferences.

Unfortunately, there are no published papers available making this commentary preliminary to future revelations. Several general principles of clinical pharmacology, pharmacokinetics, research methodology and pharmacoeconomics were useful in considering the merits of dexmethylphenidate based on the available information. Three critical questions are presented below based on the brief review of the sparse available data.

1. Do compounds with equivalent potency deliver greater effectiveness or greater tolerability? Since the single stereoisomer provides most of the desired drug efficacy while representing one-half of the total dose of the racemic mixture (*d,l*-methylphenidate), dexmethylphenidate should be used at a dosage equal to one-half the *d,l*-product. But promoting fewer milligrams per dose of the new product as if it were an advantage is problematic because it does not achieve a lower minimum effective dose of the original product. In the latter instance, a real advantage would be obtained, particularly for long-term treatments. News reports of single stereoisomer therapy suggest greater effectiveness[1] and invite conclusions of greater tolerability or purity but the detailed product information suggests that both products have similar tolerability profiles.

2. Does dexmethylphenidate have a longer duration of action than *d,l*-methylphenidate? The convenience of having once-daily dosing for school age youths is a desirable goal of the newer products. Available data describe the duration of action of dexmethylphenidate in terms of clinical ratings by parents conducted at 6pm. The significantly better parent-reported Swanson, Nolan and Pelham score at 6pm for the *d*-product compared with the *d,l*-product was the basis for suggesting that the noon dose is effective for a 6-hour duration. Mention was also made of visual analogue estimates by parents of the duration of action, although no data on the reliability of the method or results for the measure are yet available. But a longer duration is not supported by clinical pharmacology data in a study of nine boys when comparing the *d*-isomer with the racemate.[2] Additional contradictory findings relate to the wide inter-patient variability for dosage and effectiveness of *d,l*-methylphenidate[3] making it difficult to generalise from the study populations. Finally, the similarity between the *d*-isomer and the racemate in terms of more traditional outcome measures suggests that the duration of action is shorter than 6 hours (e.g. scanning response time at 5 hours post-dose for the *d*-isomer was not shown to be different from placebo[3]). Finally, the validity of the various measures and their reliability should be considered further before accepting rating scale results from the one double-blind and one noncomparative study cited here.

3. Is dexmethylphenidate likely to demonstrate therapeutic efficiency? Health systems and the prescribing physicians within them will offer dexmethylphenidate at a cost 44% above the current cost of the generic methylphenidate racemate.[4] In systems with restricted or straining dollar budgets, a critical concern is whether the *d*-isomer will deliver more effectiveness per dollar available (i.e. therapeutic efficiency) than the current product. If not, there will be fewer dollars available for other medication choices and more out-of-pocket expenses for families without any likely additional benefit.

In conclusion, the available data on dexmethylphenidate did not give evidence to support a recommendation for adopting this new product. In-

dependent assessment by the Medical Letter concurs.[4]

References

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