

NEW DRUG REVIEW

The Multimatrix Mesalamine Formulation

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In March of 2007, the US Food and Drug Administration (FDA) approved the novel multimatrix (MMX) formulation of mesalamine (Lialda, Shire) for induction of remission in patients with mild-to-moderate ulcerative colitis. The MMX formulation utilizes a gastro-resistant coating designed to dissolve at a pH of 7 in the terminal ileum. Once exposed, hydrophilic and lipophilic matrices expand and form a viscous gel mass that spreads active agent in a slow and homogeneous fashion throughout the colon. This method of release allows for once-daily dosing of oral mesalamine in the form of 2–4 pills.

FDA approval was based on the results of two studies. In the first, the investigators compared 1.2 g bid of the MMX compound for a total of 2.4 g per day, versus 4.8 g daily in a single dose, versus placebo. MMX mesalamine achieved significantly higher levels of remission than placebo, in a manner similar to other 5-aminosalicylate (ASA) studies. The subsequent study compared MMX mesalamine dosed once daily at 2.4 g, MMX once daily at 4.8 g, and 2.4 g of pH-dependent mesalamine in tid doses, all versus placebo. Again, the MMX mesalamine regimens performed significantly better than placebo in terms of achieving remission, whereas the pH-dependent formulation did not. MMX also did numerically better than the pH-dependent formulation, but the study was not powered for a head-to-head comparison of the two products.

In both studies, approximately one third of MMX-treated patients achieved clinical, and sometimes endoscopic, remission, regardless of dose or dosing regimen. The final FDA-approved dose is 2.4–4.8 g (in 2–4 pills) taken once daily, but it is possible that twice daily administration will be necessary in some patients. Importantly, there did not appear to be a difference in efficacy between 2.4 g and 4.8 g daily of the MMX preparation.

Most of the current formulations of mesalamine (pH-dependent, timed-release, or azo-bonded) require patients to take anywhere from 6–16 capsules or tablets daily. It can be off-putting for patients to take this



number of pills. Kane and associates, in their studies of patient nonadherence to 5-ASA therapy, cited pill burden as an oft-mentioned reason why patients do not take their medication. This is human nature, to which we are all subject. However, input and reinforcement from doctors is key in making it clear that maintenance therapy is necessary to prevent disease flare and maintain a normal quality of life.

My current strategy with the MMX formulation is to offer it to patients who state specific concerns about taking too many pills. Even when I explain the formulation of mesalamine pills, many patients are bothered by the concept of having to take so many pills each day. If they remain attached to this concept, the MMX formulation will provide a good alternative, particularly in the maintenance phase.

In addition, choice in medications is always a good thing, as we have seen with proton pump inhibitors (PPIs) for reflux therapy, which, theoretically, should all provide similar relief. Nonetheless, there are patients who respond to one PPI but not to another, and as physicians we must respect this concept. There are factors of individual pharmacokinetics that are not yet fully understood and it may turn out that certain patients' colons will respond to one first-line mesalamine formulation but not to another.

Suggested Reading

Lichtenstein GR, Kamm MA, Boddu P, et al. Effect of once- or twice-daily MMX mesalamine (SPD476) for the induction of remission of mild to moderately active ulcerative colitis. *Clin Gastroenterol Hepatol*. 2007;5:95-102.

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