

Delayed-Release Lansoprazole plus Naproxen

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A combination package containing lansoprazole plus naproxen has been approved for reducing the risk of NSAID-associated gastric ulcers in NSAID-requiring patients with a documented history of gastric ulcer. The indication should have also included patients with proven absence of *Helicobacter pylori* infection, as that was an inclusion requirement in the key trial. This is a very restricted indication, and would not seem to support the development and marketing of a new combination package for what is an extremely small patient group.

The combination package is likely to be widely used in an attempt to prevent major gastrointestinal complications among chronic NSAID users. Endoscopic ulcer (the endpoint in the key trial) is a surrogate endpoint for the prevention of major gastrointestinal complications. However, there is no evidence that it is a meaningful endpoint. It is potentially manipulable and increasingly suspect with regards to applicability to clinical situations.^[1] Currently, there are no data from large multicentre trials

showing the lansoprazole plus naproxen combination would achieve a significant reduction in gastrointestinal complications. The only study in high-risk patients (those who had bled from an NSAID ulcer) showed that the combination of a proton pump inhibitor and an NSAID was associated with an unacceptably high rate of rebleeding.^[2] Therefore, I would not recommend this combination for an *H. pylori*-negative patient with a recent symptomatic gastric ulcer. Instead, the recommended approach should be *H. pylori* testing and eradication if positive, avoidance of NSAIDs, or if required the combination of a cyclo-oxygenase-2 inhibitor and a proton pump inhibitor, but even that recommendation is not based on the results of large randomised trials.^[1]

In summary, since the key trial involved an extremely restricted patient group and the use of an endpoint without proven clinical applicability, I recommend that this combination package should be avoided or, at best, be used with caution for patients with the currently approved indication. ▲

References

1. Chan FK, Graham DY. Review article: prevention of non-steroidal anti-inflammatory drug gastrointestinal complications. Review and recommendations based on risk assessment. *Aliment Pharmacol Ther* 2004; 19: 1051-61
2. Graham DY. NSAIDs, *Helicobacter pylori*, and Pandora's box. *N Engl J Med* 2002; 347 (26): 2162-4