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L'ASSOCIATION CANADIENNE DE GASTROENTÉROLOGIE

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Mach 11, 2009

Ms. H. Stevenson
Assistant Deputy Minister and Executive Officer
Ontario Public Drug Programs,
Ministry of Health and Long Term Care
80 Grosvenor Street
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Dear Ms. Stevenson:

RE: Novo-5 ASA Interchangeability With Asacol

It has recently come to the attention of the Canadian Association of Gastroenterology (CAG) that the OPDP plans to deem Novo 5-ASA to be interchangeable with Asacol (400 mg tablets). Our understanding from reviewing the literature is that Novo 5-ASA has not been proven to be clinically equivalent to Asacol for the treatment of ulcerative colitis. As you can understand this is a serious concern for the CAG, it's members, and their patients, in that this may have adverse effect on patient treatment due to destabilization of previously well controlled ulcerative colitis. Given the already extremely long waiting list for patients to see a Gastroenterologist, I am certain that you will agree with our concern of yet another increased burden of unnecessary patient visits as a result of failed treatment due to inadequate therapy replacement.

Effective treatment of ulcerative colitis depends upon the predictable and reliable delivery of 5-ASA to the large intestine. This drug acts via a topical effect and any of the drug that is absorbed in the proximal small bowel, does not reach the colon for adequate treatment effect. To ensure optimal delivery to the colon, a variety of delivery mechanisms have been used, including special pH sensitive pill coatings (Eudragit S in the case of Asacol), which exploit the dramatic pH difference between the small bowel and colon. Thus, from our point of view, any drug deemed to be equivalent to Asacol must demonstrate equivalent delivery of equimolar amounts of drug to the colon under fasting, fed, and disease state conditions. We do not believe that these conditions exist for Novo-5 ASA as demonstrated by the following:

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1. Release of active drug from the Novo 5-ASA tablet occurs below a pH of 7.0. The product monograph for Novo-5 ASA suggests that release of active 5-ASA can occur at pH's significantly below 7.0. The concern with this is that significant small bowel absorption of 5-ASA will occur resulting in less delivery of active drug to the colon. In patients who are on a stable dose of Asacol for maintenance therapy of chronic ulcerative colitis, a switch from Asacol to Novo 5-ASA could result in a flare of disease as there will be a reduction in the amount of active drug delivered to the site of inflammation.
2. Novo 5-ASA has been examined for bioequivalency by other regulatory bodies including Saskatchewan Health and Health Canada. These organizations have conducted their own independent investigations including laboratory dissolution studies and have concluded that Novo 5-ASA fails to meet adequate standards. As a result, no province in Canada to this point has deemed Novo 5-ASA and Asacol to be bioequivalent.
3. There is no clinical trial evidence for Novo 5-ASA in the treatment of Ulcerative Colitis. Clinical trials examining the efficacy of various 5-ASA products in the treatment of chronic ulcerative colitis have demonstrated considerable differences in efficacy based on different delivery methods. For example, products that are designed for release in the small bowel (as was intended for the treatment of Crohn's disease) may require higher doses to be effective in the treatment of ulcerative colitis. Thus, it is incumbent upon the drug manufacturer to prove that their product is in fact effective for the treatment of ulcerative colitis. To our knowledge, Novo 5-ASA has never been subjected to the rigor of a published clinical trial either for treatment of acute flares of ulcerative colitis or as chronic maintenance therapy.

The ODPD intention of bioequivalence designation means that pharmacists will be able to substitute Novo 5-ASA for Asacol without the attending physician's knowledge. We are unable to endorse this policy as it will have an adverse effect on patient care and will result in increased use of health care resources.

We look forward to dialoguing with you on this very important issue.

Sincerely yours,

Daniel C. Sadowski, MD, FRCP(C)
Vice President, Clinical Affairs

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