

October 27, 2005

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 78N-036L

Dear Sir or Madam:

On December 10, 2003 Braintree Laboratories sent a letter to this docket commenting on a C.B. Fleet Citizens Petition (1978N-0036L/CP28) filed June 25, 2003 concerning labeling changes to allow double dose administration of their sodium phosphate solution for bowel cleansing. In our letter, we discussed the persistent problem of electrolyte abnormalities (particularly severe hyperphosphatemia, hypokalemia and hypocalcemia) which typically result from use of sodium phosphate bowel preparations. In particular, we discussed a 2003 New England Journal of Medicine publication by Desmules et al. (copy attached) which reported on a patient that developed renal failure and calcification of the kidney (nephrocalcinosis; as determined by kidney biopsy) following the use of sodium phosphate based cathartics for bowel cleansing prior to colonoscopy. The authors of that report noted that the patient suffered a permanent degradation of kidney function as assessed by pre and post preparation serum creatinine levels.

In a recent publication by Markowitz et al. (copy attached), records from patients that had had renal biopsies processed at Columbia University over a 5 year period were reviewed. Of 7349 biopsies, 31 cases of nephrocalcinosis in the absence of hypercalcemia were identified. Twenty-one (68%) of these cases had presented with acute renal failure and also had a recent history of bowel cleansing for colonoscopy with a sodium phosphate cathartic (Fleet Phosphosoda or Visicol). The mean age of these patients was 64 years (six patients were 55 or younger) and most were female. Before bowel cleansing, serum creatinine levels were normal (<1.2 mg/dl) in 17 of these patients and the remaining 4 had mild renal insufficiency (serum creatinine <1.7). Most alarming is that by an average of 4 months after colonoscopy the mean serum creatinine level for all 21 patients was significantly abnormal at 3.7 mg/dl. Four patients eventually developed end stage renal failure requiring hemodialysis (only one of which had had elevated serum creatinine at baseline). Similar to the Desmuelles report, the remaining 17 patients sustained permanent kidney damage with a mean serum creatinine level of 2.4 mg/dl by about 16 months after colonoscopy.

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As stated in our letter of December 10, it is clear that sodium phosphate purgative labeling is inadequate to address the continuing problems resulting from the electrolyte derangements and volume depletion caused by these products. As demonstrated by DiPalma et al. (1996, copy attached) the calcium-phosphorus solubility product (CaXP) greatly exceeds the normal range after each dose of sodium phosphate prep (see Table 2 in that reference). Markowitz and coauthors may have answered the question as to what ultimately happens to calcium phosphate complexes that form in patient serum as a result of acute hyperphosphatemia.

Sincerely,

A handwritten signature in cursive script that reads "Mark vB. Cleveland". The signature is written in black ink and is positioned above the printed name.

Mark vB. Cleveland, Ph.D.
Vice President
Regulatory and Scientific Affairs