INTRODUCTION

- Nefacon, a novel oral formulation of the corticosteroid budesonide, is specifically designed to target release in the Peyer’s patch-rich distal ileum, a major source of Gl-IgA1 overproduction.
- Nefacon is not currently approved by the FDA and EMA for adult patients with primary IgA1 at risk of rapid disease progression.1

Three other oral budesonide formulations are commercially available: Entocort, Budesofenate, and Corticentre.2,3
- They are used for the treatment of inflammatory bowel diseases such as Crohn’s disease and ulcerative colitis.
- Each formulation is designed to selectively target a specific disease and, hence, the relevant part of the gastrointestinal tract.
- The aim of this study was to compare the dissolution of budesonide from the four formulations to ascertain their interconvertibility.

METHODS

- Dissolution experiments were performed to compare the release of budesonide from each formulation.
- Products were subjected to an acidic environment for 2 hours, representing maximum residence time in a fasted stomach.
- This was followed by exposure for 3 hours to a buffer environment, representing passage through the small intestine.
- Two sets of experiments were performed:
  - Standard USP quality control design conditions (Method B),1 with a pH of 6.8 in the intestinal phase.
  - A biorelevant method, with a pH of 6.5 in the intestinal phase and using a lower concentration of buffer to better reflect the in vivo intestinal environment.
- Samples were analyzed using ultra-high performance liquid chromatography.

- No formulation released significant amounts of budesonide in the acid (gastric) phase of the experiment; therefore, only data for the buffer (intestinal) phase are shown.
- For Nefacon, capsule disintegration and onset of budesonide release occurred 1 hour after entering the buffer phase.
- Budesofenate was released over a relatively short period, starting at 1 hour and completing by 3 hours.
  - This release pattern corresponds to a localized release of budesonide to the Peyer’s patch-rich ileum.
- Entocort started releasing budesonide almost immediately upon entering the buffer phase due to the low pH level of the entero-coating.
  - Its release lasted over 3 hours, with almost 80% released in the first hour; the remaining 20% would mostly be released in the proximal small intestine.
- Corticentre did not release budesonide in the biorelevant method medium over the 3-hour period.
  - In the higher pH standard USP buffer, Budesofenate released budesonide after a 2-hour delay.
  - This would be consistent with some budesonide release in the terminal ileum, but with transfer of a substantial amount to the colon.
- Corticentre failed to release budesonide in the intestinal phase with either method, suggesting that release starts in the colon in accordance with its LIC indication.
- All f2 values were <50, failing to meet the criterion for similarity between dissolution profiles by a wide margin.

RESULTS

CONCLUSIONS

- The doses, dosing conditions, and approved indications of the four budesonide products differ widely, and this study demonstrated that each formulation has a distinct dissolution profile consistent with its individual therapeutic goals.
- The rapid release of budesonide from Nefacon after 1 hour in intestinal conditions is expected to result in a localized release of budesonide to the Peyer’s patch-rich ileum, the target tissue for downregulation of Gl-IgA1 production.
- The f2 analysis demonstrates strongly dissimilar release profiles, showing that there is no basis for the formulations to be considered pharmacologically or therapeutically interconvertible.

REFERENCES