Physicochemical Stability of Pantoprazole 2 mg/mL Oral Suspension in SuspendIt®

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INTRODUCTION

Pantoprazole is a proton pump inhibitor commonly given by mouth or by intravenous injection/infusion in the treatment of gastro-oesophageal reflux disease, gastric/duodenal ulcers and dyspepsia. The commercially available gastro-resistant tablets are not licensed for use in children and do not permit age/weight adjustments of the dosage strength [1]. As such, an alternative extemporaneous preparation was developed for pantoprazole 2 mg/mL in the proprietary vehicle SuspendIt, which is sugar-free, paraben-free and gluten-free, and thus appropriate for the paediatric population. The Beyond-Use Date (BUD), time from the date of preparation after which a compounded medication may no longer be used, was determined by testing the physicochemical stability of the oral suspension.

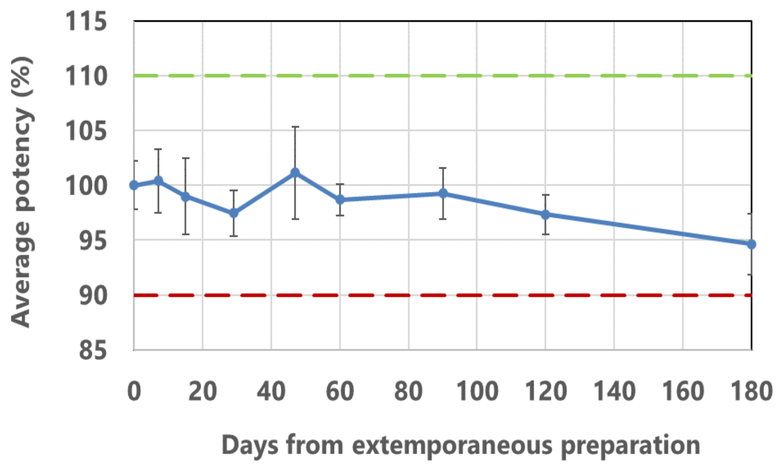
MATERIALS & METHODS

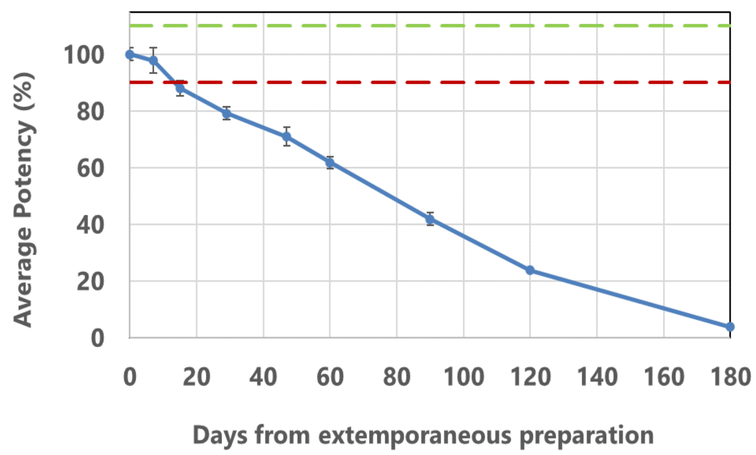
A batch of 500 mL was prepared for pantoprazole 2 mg/mL by triturating Pantoprazole Sodium Sesquihydrate USP 1.13 g and Sodium Bicarbonate USP 55 g to a fine powder. Part of SuspendIt was added to the powders (about 15% of final volume), and mixed well until a smooth paste, free of lumps was formed. The Polysorbate 20 NF 1 mL was then added to the paste and mixed well. The preparation was transferred to a 150 mL beaker equipped with a SpinBar and SuspendIt was added until about 95% of final volume. The pH was adjusted to 8.0-8.5 with Sodium Hydroxide 10% (W/V) Aqueous Solution dropwise and the final volume was completed with the remainder SuspendIt. The oral suspension was distributed into 30-mL amber plastic bottles and the study samples were then stored for 180 days in a laboratory refrigerator at a temperature of 5^0C ± 3^0C; and in an environmentally controlled chamber at a temperature of 25^0C ± 2^0C and relative humidity of 60% ± 5%. The physical characterization consisted in observing all samples for appearance/color and odor, and testing for pH (Horiba LaquaTwin pH meter) and density (Mettler-Toledo Density Excellence D4). The chemical characterization consisted in a validated, stability-indicating Ultra-High Performance Liquid Chromatography (UHPLC) assay testing (Waters Acquity). At pre-determined time points [0 (baseline), 7, 15, 29, 47, 60, 90, 120 and 180 days], a study sample (one unopened bottle) was withdrawn from the storage conditions, shaken vigorously and tested for physicochemical stability.

RESULTS AND DISCUSSION

Considering the physical characterization, the pantoprazole oral suspension stored at refrigerated temperature exhibited a homogeneous pale-yellow color and an opaque, smooth appearance, as shown in Figure 1 (right). The range of densities (1.0550-1.0712 g/mL) and the range of pH (8.30-8.65) were within the acceptable limits. On the other hand, the pantoprazole oral suspension stored at room temperature exhibited a remarkable change of color, from pale-yellow to dark brown, over the 180 days of the study, as show in Figure 1 (left). The range of densities and the range of pH were as follows: 1.0433-1.0743 g/mL and 8.39-8.72. Considering the chemical characterization, the chromatographic assay method was validated by evaluating the system suitability, linearity, accuracy, precision (repeatability and intermediate), robustness, solution stability, and specificity. Subsequently, the percent potency was calculated taking into account the baseline measurements on day 0. The potency of the oral suspensions remained within the ±10% specifications [2] throughout the study for the refrigerated temperature only: 94.7% - 101.1% (Figure 2). For the room temperature, the potency was below the limits from day 15 (88.1%) onwards (Figure 3). As a result, the pantoprazole oral suspension is physically and chemically stable at 5°C (only) for 180 days in amber plastic bottles.

Figure 1. Study samples of pantoprazole 2 mg/mL oral suspensions stored at 5^0C (right) and 25^0C (left) by day 120 of the stability study.





Figures 2 and 3. Average percent potency of the pantoprazole oral suspension 2 mg/mL stored at 5^0C (Fig. 2, left) and 25^0C (Fig. 3, right) over 180 days from extemporaneous preparation. The green and red dotted lines show the ±10% upper and lower limits, respectively.

CONCLUSIONS

The BUD of the pantoprazole 2 mg/mL oral suspension in SuspendIt is 6 months at refrigerated temperature, in amber plastic bottles.

References:

1. Joint Formulary Committee (2021) British National Formulary 81. London: BMJ Group and Pharmaceutical Press. Available at: http://www.medicinescomplete.com (Accessed: 15 May 2022).

2. The United States Pharmacopeial Convention (2016) 'General Requirements / <2> Oral Drug Products – Product Quality Tests'. USP 39 – NF 34. Rockville: USP, p.77.