Stability of Extemporaneously Compounded Domperidone 5mg/mL Suspension

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INTRODUCTION

Domperidone is a dopamine antagonist with antiemetic and gastro-prokinetic properties. It increases the lower esophageal sphincter pressure, esophageal peristalsis and gastric emptying. It decreases small bowel transit time. Domperidone is used in patients requiring a gastrointestinal motility-enhancing agent.

OBJECTIVES

The objective of this study was to evaluate the stability of domperidone 5 mg/mL suspensions stored in amber glass bottles, amber plastic PET and amber plastic PVC bottles at both 23 C (RT) or 4 C and plastic oral syringes at 23 C (RT) only using Oral Mix vehicle.

METHODS

The concentration of domperidone in bottles (23 C and 4 C) and syringes (23 C) was evaluated during storage at each temperature using a validated stability indicating liquid chromatographic method using UV detection.

Stability Study: Bottles and Syringes at 23 C and 4 C

On study day 0, three separate 500mL batches of domperidone 5mg/mL suspensions were prepared with Oral Mix (Medisca) and domperidone 10mg tablets (Ranbaxy). Each 500mL batch was divided into 6x75mL and placed in 100mL or 250mL size amber glass, amber PET and amber PVC bottles (allows airspace) for a total of 18 bottles. Half of the bottles were stored at room temperature (23 C, exposed to ambient light), the other half were refrigerated (4 C). Also, from each of the 3 batches, 50mL of the suspension was drawn into 3mL oral syringes (45 syringes in total) which were stored at room temperature (23 C). Samples from bottles and syringes were analyzed by HPLC in duplicate at days 0, 1, 2, 4, 7, 10, 14, 21, 28, 35, 42, 49, 56, 72 and 91.

Data Reduction and Statistical Analysis

Analysis of variance was used to test differences in concentration on different study days, at different temperatures and in different bottle containers. The 5% level was used as the a priori cut-off for significance. Domperidone concentrations were considered acceptable or ‘within acceptance limits’ if the lower limit of the 95% confidence limits on concentration remaining was greater than 90% of the initial (day 0) concentration.

RESULTS

Table 1. Refrigerated (4 C) Studies

<table>
<thead>
<tr>
<th>Study Day</th>
<th>PVC</th>
<th>Glass</th>
<th>PET</th>
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<td>5 mg/mL</td>
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<td>100.00</td>
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<td>96.82</td>
<td>99.42</td>
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<td>56</td>
<td>94.95</td>
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Data at 70% (days) % remaining on day 91 based on fastest degradation rate (95% CI)

Table 2. Room Temperature (23 C) Studies

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CONCLUSION

Extemporaneous oral domperidone 5 mg/mL suspensions assessed above 93% of the initial concentration for 91 days when stored in 3 types of containers (amber glass, PET, and PVC) at 2 different temperatures (23 C and 4 C) and oral syringes at 23 C. However, the best determination with most confidence for assigning an expiry date is based on the percent remaining using the fastest degradation rate with 95% CI. On day 91, PVC and glass bottles (4 C, 23 C) more than 93.15% and 90.84% remained respectively. PET bottles were less stable at 23 C (88.80%) than at 4 C (92.14%) and syringes had only 87.81%.

Refrigeration will reduce the degradation rate and minimize bacterial growth. Since domperidone degradation in bottles at 4 C results in more than 90% remaining after 91 days of storage with 95% confidence, we recommend storage of suspensions in glass, PVC or PET at 4 C for no more than 91 days. Suspensions stored in oral syringes at room temperature should not exceed 74 days.