Establishing a Beyond Use Date for Compounded Marbofloxacin Oral Suspension

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Abstract

Purpose: USP General Chapter <795> requires a Beyond Use Date (BUD) for all compounded pharmaceutical preparations. In the absence of literature data, the maximum BUD that can be assigned for an oral aqueous suspension is only 14 days. The study was conducted to determine a BUD for Compounded Marbofloxacin Oral Suspension (MOS) in three conventional suspension vehicles stored at ICH conditions up to 3 months.

Methods: MOS was compounded in three conventional suspension vehicles. Formulations were prepared on the day of testing. A 12 week stability study was conducted to assess the stability of compounded Marbofloxacin Oral Suspension in three conventional suspension vehicles stored at ICH conditions up to 3 months.

Compounding
Marbofloxacin Oral Suspension 20 mg/mL was compounded in three vehicles for sample comparison: Orabell, OralSweet/OraPlus 1:1, or Syrup NF. Each suspension was compounded by grinding twenty (20) marbofloxacin tablets (equivalent to 2 g marbofloxacin) in a mortar with a pestle into a coarse powder. Film coating was separated by passing the ground material through a 10 mesh screen. The screened powder was returned to the mortar and further ground into a fine powder, wetted with a few drops of glycerin NF, then triturated with small portions of vehicle to obtain a smooth paste. Increasing volumes of the vehicle were added geometrically to obtain a pourable liquid. The compounded suspension was transferred to a 100 mL volumetric flask, rinsing the mortar several times with additional vehicle, then bringing to final volume with 100 mL vehicle.

Materials
Marbofloxacin 100 mg tablets (Zeniquin® lot # PF08085, Pfizer Animal Health) and OraBlend (lot # 1356750, Paddock Labs) were used as received. OraSweet (lot # 1417226, Paddock Labs) and OraPlus (lot # 1417226, Paddock Labs) were compounded as required. Syrup NF (compound) was used as received.

HPLC Analytical Method
A high performance liquid chromatography (HPLC) method was developed for measuring marbofloxacin content in Marbofloxacin Oral Suspension based on the USP monograph for Marbofloxacin. The conditions used for sample analysis were:
- Column: Supelco Discovery® C18, 5μm, 250 x 4.6mm
- Column Temperature: 40°C, +/- 1°C
- Injection volume: 10 μL
- Flow Rate: 1.0 mL/min
- Pump Program: Isocratic
- Detector: UV absorbance at 300 nm
- Mobile Phase: ACN:0.1% H3PO4 (10:90)
- Sample Diluent: 0.02M, pH 7.0 phosphate buffer

Results & Discussion

Results: The stability data are presented in graphical format in Figures 3-6. Regression analysis was conducted on the data and a 95% confidence interval (CI) was calculated. The 95% CI around the stability data indicates a predicted BUD where the lower or upper CI crosses the specification limit of 90% or 110% of labeled content (20 mg/mL), respectively.

Based on this 90 day stability study, only the OralSweet/OraPlus formulation provided support for the assignment of a BUD beyond the default 14 days specified in USP <795> for aqueous preparations. The OralSweet/OraPlus data (Figure 4) predict a BUD of ~18.5 weeks. Based on this data a 60 day BUD is recommended for Marbofloxacin Oral Suspension compounded in OralSweet/OraPlus and stored at controlled room temperature.

Conclusions
Stability studies were conducted on three different formulations: OraBlend, OralSweet/OraPlus, and Syrup NF for Compounded Marbofloxacin Oral Suspension. The stability data support assignment of a 60 day BUD for Compounded Marbofloxacin Oral Suspension when stored at controlled room temperature. The suspension should not be refrigerated.

Disclosure
St. Elder is a member of the 2010-2015 USP Compounding Expert Committee. Information presented should not be construed as an official explanation or interpretation of USP Standards.