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Poster Title: Chemical and physical compatibility of revefenacin inhalation solution mixed with either albuterol sulfate, arformoterol tartrate, or budesonide

Purpose: Revefenacin inhalation solution is a long-acting muscarinic antagonist indicated for maintenance treatment of chronic obstructive pulmonary disease (COPD). Once daily dosing of revefenacin may be convenient, however, there is a lack of compatibility data on mixing revefenacin with other inhalation solutions to be administered via nebulizer. Simultaneous nebulization of prescribed inhalation solutions is both preferred and practical. At Atlanticare Regional Medical Center, revefenacin was added to our formulary, and compatibility issues have been raised by our respiratory therapists. The purpose of the study is to determine the compatibility of revefenacin inhalation solution when combined with albuterol sulfate or arformoterol tartrate.

Methods: Two-drug admixtures were prepared by mixing one vial of revefenacin solution (175 mcg/3 mL) with one vial of albuterol sulfate (2.5 mg/3 mL), one vial of arformoterol tartrate (15 mcg/1 mL), or one vial of budesonide (0.5 mg/3 mL; Nephron Pharmaceuticals Corporation). Triplicates of each admixture were prepared in glassware and solutions were gently mixed for one minute to achieve homogeneity. Triplicates of each admixture were prepared in glassware and solutions were gently mixed for one minute to achieve homogeneity. The pH of each solution was measured and visual inspection was performed immediately after mixing (time zero [T0]), at 30 minutes (T30), at 60 minutes (T60), and at 360 minutes (T360) at an ambient room temperature of 23.7 degrees Celsius. Additionally, one admixture of revefenacin plus albuterol or arformoterol was nebulized at T0 to inspect for changes in the physical characteristics of the solutions and to approximate the time to complete a nebulization treatment. A calibrated pH-100 meter, standard jet nebulizer, and small volume nebulizer were utilized in this study. Physical compatibility was defined as a pH variation of less than or equal to 10 percent and no visual evidence of physical solution changes at T0 versus T30 and T30 versus T60. Physical solution changes were determined by visual inspection, defined as evidence of precipitation, turbidity, and/or discoloration. Nebulized admixtures were considered compatible if there were no remarkable changes in the physical characteristics of the mixed solutions.

Results: Compatibility acceptance criteria were met for revefenacin when mixed with either albuterol sulfate, arformoterol tartrate, or budesonide. At T0, T30, T60, and T360 visual inspection of the triplicate solutions were clear, colorless, with no precipitation. The mean pH of the revefenacin and albuterol admixture was 5.29 +/- 0.08 at T0, 5.27 +/- 0.02 at T30, 5.29 +/- 0.01 at T60, and 5.36 +/- 0.05 at T360 with a pH difference of -0.4 percent at T0 versus T30 and 0.4 percent at T30 versus T60. The mean pH of the revefenacin and arformoterol admixture was 5.31 +/- 0.06 at T0, 5.23 +/- 0.02 at T30, 5.32 +/- 0.03 at T60, and 5.26 +/- 0.01 at T360.
with a pH difference of -1.6 percent at T0 versus T30 and 1.7 percent at T30 versus T60. The mean pH of the revefenacin and budesonide admixture was 4.85+/- 0.05 with a pH difference of -0.03 percent at T0 versus T30 and 1.0 percent at T30 versus T60. The physical characteristics of each nebulized drug admixtures starting at T0 were unremarkable, producing a homogenous vaporized mist that was colorless with no observed crystallization. The approximate nebulization time was 30 minutes for revefenacin plus albuterol, 25 minutes for revefenacin plus arformoterol, and 10 minutes for revefenacin plus budesonide. The notable variance in nebulization time is attributed to using a different nebulization device for the revefenacin and budesonide admixture. Approval by our institutional review board was deemed unnecessary for this study.

**Conclusion:** Under our study methodology, revefenacin proved to be physically and chemically compatible when mixed with albuterol sulfate, arformoterol tartrate, or budesonide for at least 60 minutes at room temperature. The ability to simultaneously nebulize revefenacin with albuterol or arformoterol serves as an administrative convenience for both patients and healthcare professionals. Further research is warranted to determine the compatibility of revefenacin with other inhalation solutions indicated for the treatment of COPD.