Stability and Sterility of Tildren®
(tiludronate disodium) ***Post-Reconstitution***

White paper

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White paper:
Stability and sterility of Tildren®
(tiludronate disodium) after reconstitution

Problem:

Tildren® (tiludronate disodium) was launched in 2014 in the United States as a single vial containing 500mg of tiludronate disodium as a powder. Prior to use, the powder is reconstituted with 25mL of 0.9% sodium chloride and the resulting solution is administered via intravenous infusion at a rate of 1.0 mg/kg. Once reconstituted, a single vial of Tildren will treat horses weighing up to 1,210 lbs. The question addressed in this white paper is the chemical stability and microbial quality of Tildren after reconstitution.

Why:

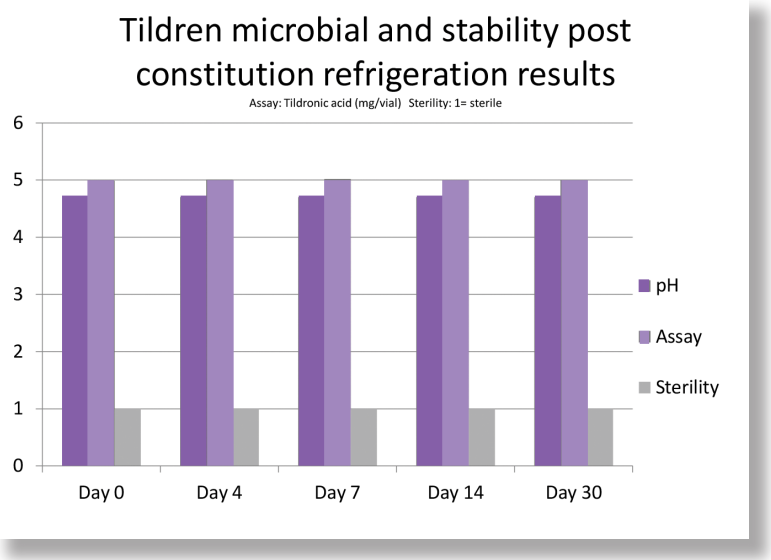
The objective was to know whether a partially used reconstituted bottle of Tildren maintained during short term storage under controlled conditions is of suitable quality to be used within a specified period of time. With a single 500mg vial of Tildren treating horses weighing up to 1,210 lbs, a veterinarian treating a 600 lb pony with navicular disease would require only 15mL of the reconstituted solution and would have 10mL left over. In the same vein, a veterinarian treating a 1,350 lb. warmblood would require 30 mL, one full vial of 25mL plus 5mL from a second vial. Again, there would be reconstituted product (20mL) left over. This study examined whether reconstituted Tildren could be stored under controlled conditions and reused, to minimize waste.

Test Design:

This post-approval research* was conducted to evaluate the stability and microbial quality of reconstituted Tildren when stored for up to 30 days at three different temperatures: climatic controlled room temperature (25°C), refrigerated (5°C) and frozen (-20°C). The frozen sample was thawed at room temperature.

Tildren was reconstituted according to label directions using a sterile syringe and 25mL of sterile 0.9% sodium chloride. After shaking to dissolve the powder, it was placed into one of three climate controlled chambers. Serial samples were collected at specific times for evaluation using a sterile syringe and needle. Physico-chemical analysis was conducted at Day 0, Day 4, Day 7, Day 14 and Day 30, and sterility tests were conducted on all vials at the end of the study (Day 30).

Results:



After 30 days of storage, Tildren showed:

No decrease in the concentration of tiludronic acid
No generation of degradation products
Partially used solution remained sterile over 30 days
The physical characteristics remained unchanged (appearance & pH)

Conclusions:

The findings from storage at all three temperatures - room temperature, refrigeration and freezing - were nearly identical. As a result, the quality of a partially used reconstituted vial of Tildren maintained under short term storage at either -20°C, 5°C or 25°C is suitable for use within 30 days.

Discussion:

In cases that necessitate the use of a partial vial of reconstituted Tildren, we recommend the solution be withdrawn in a sterile manner and the remainder labeled with the date of reconstitution and maintained protected from light in the refrigerator for up to 30 days. This will facilitate the ease of accurate dosing while minimizing waste.

* Data on file

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