19th Congress of the EAHP

Barcelona, 26 - 28 March 2014

# Physico-chemical stability of cabazitaxel containing premix solution and ready-to-administer solutions

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## Objectives

This study was conducted to investigate the extended physico-chemical stability of cabazitaxel containing premix solution and diluted infusion solutions using either 0.9% sodium chloride (NaCl) or 5% glucose (G5) infusion solution as vehicle solution.

## Materials and Methods

Test solutions and sample preparation

- Premix solutions of cabazitaxel were prepared in the original vials. Test solutions were prepared in triplicate. Samples were diluted with water for injection to fit the calibration curve.
- Infusion solutions of the recommended minimum and maximum cabazitaxel concentrations (0.1 mg/mL, 0.26 mg/mL) were prepared by adding the calculated volume of cabazitaxel premix solution in prefilled PP/PE infusion bags with 0.9% NaCl or 5% glucose (freeflex® 100 mL bags, Fresenius Kabi). Infusion solutions were prepared in triplicate.
- Test solutions were stored over a period of 28 days. Samples were taken at predefined time points and assayed in triplicate.

Storage conditions:

- refrigerated (2 – 8 °C)
- room temperature (25 °C) protected from light

Physical stability:

- measurement of pH value and visual inspection

Chemical stability:

- quantitative analysis of cabazitaxel by reversed-phase high-performance liquid chromatography (RP - HPLC)-assay with ultraviolet detection:
- HPLC-System: Waters 717 plus Autosampler, Waters 510 HPLC-pump, Waters 996 photodiode array detector, Waters Empower Pro-Software
- Column: Hypersil ODS C18 150 x 4.6 mm, 5 µm
- Mobile phase: 60% acetonitrile : 40% water HPLC grade
- Flow rate: 1.2 mL/min
- Injection volume: 10 µL
- Evaluation wavelength: 230 nm

Concentrations above 90% of the initial cabazitaxel value were considered as chemically stable.

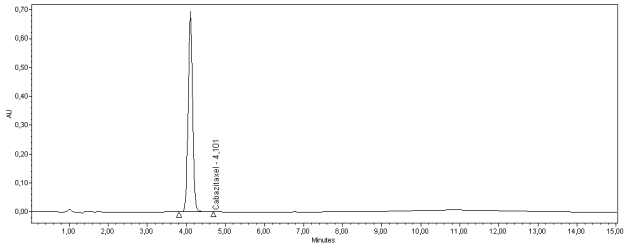


Figure 1: HPLC-chromatogram of 0.3 mg/mL cabazitaxel

## Results

**Chemical stability**

- Detailed results for the premix (nominal concentration 10.0 mg/mL) are shown in the Table 1.
- Detailed results for the diluted solutions are shown in Figure 2 (nominal concentration 0.1 mg/mL) and Figure 3 (nominal concentration 0.26 mg/mL).
- Concentrations did decrease only insignificantly, besides crystallization took place.

**Physical stability**

- pH values varyed from pH 4.23 to 5.77 dependent on the amount of cabazitaxel and dilution medium and remained unchanged over 28 days (data not shown) .
- Precipitation occured in particular infusion solutions beginning at day 21.

Table 1: Premix solution (10 mg/mL cabazitaxel)

| Storage temperature | 25 °C | 2 - 8 °C |
|---|---|---|
| Initial measured concentration [mg/mL] | **10.89** ± 2.1 | **10.77** ± 2.0 |
| | Remaining concentration expressed as percentage rate [%] of the initial concentration ± RSD, mean of triplicate assays of 3 test solutions, n=9 if not otherwise indicated | |
| Day 1 | **97** ± 2.3 [1] | **98** ± 2.4 [2] |
| Day 7 | not available due to technical problems | |
| Day 14 | **100** ± 1.4 | **97** ± 3.1 |
| Day 21 | **99** ± 5.2 | **100** ± 4.9 |
| Day 28 | **101** ± 1.9 | **102** ± 2.1 |

[1]: n= 8, [2]: n=6

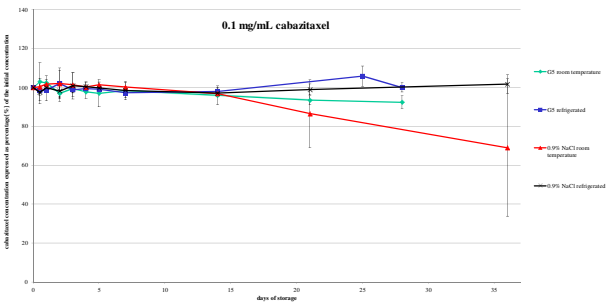


Figure 2: 0.1 mg/mL cabazitaxel in 5% glucose and 0.9% NaCl stored at room temperature or refrigerated

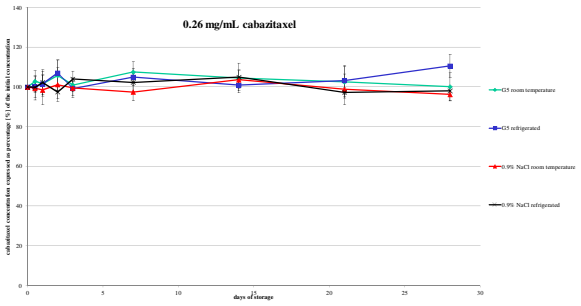


Figure 3: 0.26 mg/mL cabazitaxel in 5% glucose and 0.9% NaCl stored at room temperature or refrigerated

## Conclusions

Cabazitaxel premix solutions and cabazitaxel infusion solutions prepared with 0.9% NaCl or 5% glucose solution as vehicle solutions in PP/PE bags are chemically stable over a storage period of 28 days either refrigerated or stored at room temperature protected from light.

Diluted infusion solutions should be visually checked prior to use as unpredictable crystallization of cabazitaxel may occur.

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