Physicochemical stability of etoposide diluted at range concentrations between 0.38 and 1.75 mg/mL in polyolefin bags

Elise D'Huart,¹ Jean Vigneron,¹ Pauline Lider,¹ Béatrice Demoré^{1,2}

¹Pharmacy, University Hospital, Vandoeuvre-lès-Nancy, France
²University of Lorraine, EA 4360 APEMAC, Nancy, France

Correspondence to

Elise D'Huart, Pharmacy Department, University Hospital, Allée du Morvan, 54511 Vandoeuvre-lès-Nancy, France; dhuartelise@gmail.com

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ABSTRACT

Introduction According to the manufacturers, the diluted solution of etoposide should not exceed 0.4 mg/mL because precipitation may occur. For high doses or for patients requiring fluid restrictions, etoposide phosphate may be an option but shortages occurs frequently. The objective of this work was to study the stability of etoposide solutions between 0.38 and 1.75 mg/mL, diluted in 0.9% sodium chloride (0.9% NaCl) or 5% glucose (G5%) in polyolefin bags, stored at 25°C and between 2°C to 8°C, in a 61-day period. This study also observed the impact of an infusion pump on the physical and chemical stability of etoposide solutions.

Materials and method Chemical stability was analysed at days 0, 9, 16, 21, 28 and 61 by high-performance liquid chromatography. Physical stability was evaluated by visual and subvisual inspection. The action of an infusion pump on solutions was evaluated to verify the impact of the mechanical pumping action on the etoposide solutions. This investigation was performed at day 61, at the end of the study.

Results Etoposide solutions diluted at 0.38, 0.74 and 1.26 mg/mL in G5% and stored at 25°C were stable for 61 days and at 1.75 mg/mL for 28 days. In 0.9% NaCl, etoposide was less stable, with more precipitations observed. The action of an infusion pump has not caused any physical modifications.

Conclusion Storage at 25°C and G5% as diluent are recommended for etoposide high concentration with 61-day stability up to a concentration of 1.26 mg/mL and 28-day stability up to a concentration of 1.75 mg/mL. As a precaution, the use of an administration set with an in-line micro-filter is nevertheless recommended. Storage at 2°C to 8°C and the use of 0.9% NaCl increase the risk of precipitation.

INTRODUCTION

Etoposide is a semisynthetic derivative of podophyllo-toxin. The commercially available etoposide injection is formulated in a mixture of alcohols and surfactants due to poor water solubility: polysorbate 80, polyethylene glycol 300, benzyl alcohol, citric acid and ethanol. Etoposide is highly lipophilic. Another formulation of this drug is marketed: the phosphate ester of etoposide (Etopophos, Bristol Myers Squibb). The advantage is its high solubility in water. However, Etopophos has frequent shortages, which limits its use. One vial of Etoposide 200 mg 10 mL (Mylan) costs around 4 euros. While for an equivalent dose, two vials of Etopophos 100 mg (Bristol Myers Squibb) cost around 60 euros.

This cytotoxic drug is used to treat several malignancies including non-Hodgkin and Hodgkin lymphoma, small cell lung cancer and ovarian carcinoma.

The manufacturers determined a 96-hour stability for the etoposide diluted at 0.2 mg/mL up to 48 hours for 0.4 mg/mL etoposide solutions at 25°C. Summaries of product characteristics specify that etoposide needs to be diluted with 5% glucose or 0.9% sodium chloride (0.9% NaCl) with volumes ranging from 250 to 1000 mL. The final concentration should not exceed 0.4 mg/mL and diluted solutions should not be stored in the refrigerator because precipitation may occur.^{1,2}

Stability studies of 0.4 mg/mL etoposide solutions were reported in a number of previous publications. Barthes et al recommended that 0.4 mg/mL solutions of etoposide should not be stored more than 24 hours at 25°C and 2°C to 8°C.³ Joel et al determined a 7-day stability for 0.4 mg/mL etoposide solution in polyvinylchloride (PVC) bags, at 25°C in 0.9% NaCl and 5% glucose.⁴ Beijnen et al determined a 4-day stability for etoposide solutions at 0.4 mg/mL at 25°C in 0.9% NaCl, 5% glucose and Ringer lactate.⁵ Lepage et al reported that 0.4 mg/mL etoposide was stable for 2 days at 2°C to 8°C and 24 days at 25°C. They reported that 10 mg/mL etoposide was stable for 7 days at 2°C to 8°C and 5 days at 25°C. Between concentration ranges from 2 mg/mL to 10 mg/mL, they studied only the physical stability and they observed the formation of precipitates.⁶

The recommended dose of etoposide is 60 to 120 mg/m² administered by intravenous infusion (IV) daily for 3 to 5 days over 30 to 60 min.¹ Sometimes, the dose may increase up to 300 mg/m² for the treatment of non-Hodgkin's lymphoma. For patients with a body surface area of 2 m² (slightly above the mean value for women and men), the dose of etoposide will be 600 mg. This solution should be diluted with 1.5 litres of solvent so as not to exceed a concentration of 0.4 mg/mL. This fluid intake is not always feasible for patients. For these high doses, the etoposide phosphate salt, Etopophos, can be used without concentration limits. In fact, for a dose of 300 mg/m² and a patient with a body surface area equal to 2 m², the volume of dilution can be 250 mL.⁷

Woloschuk et al observed in etoposide solutions extensive white precipitates in the intravenous tubing below the pumping chamber.⁸ The manufacturer suggested that in-line precipitation of etoposide may occur at etoposide concentrations equal to, or higher than, 0.4 mg/mL if solutions are infused using a peristaltic mechanism infusion

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device. As etoposide, paclitaxel is extremely lipophilic and this causes difficulties in developing stable parenteral infusion. Pfeifer et al observed white precipitates in paclitaxel solutions throughout the section of tubing distal to the peristaltic pump.⁹ They suggested that 'agitation sufficient to induce precipitation could be produced by mechanical pumping action'. Bogardus et al have reported similar problems with teniposide, which is chemically similar to etoposide.¹⁰ Manufacturers precised that 'supersaturated solutions of teniposide rapidly precipitate after formation of seed crystals. This process may be accelerated by agitation'.

The first objective of this work was to study the stability of etoposide in 0.9% NaCl and 5% glucose over a range of concentrations equal or higher than the recommended limit concentration at 0.4 mg/mL, (0.38 mg/mL to 1.75 mg/mL) at 25°C and between 2°C to 8°C after 9, 16, 21, 28 and 61 days in polyolefin bags. Stability data at higher concentrations of etoposide than 0.4 mg/mL would overcome Etopophos shortage. That would facilitate the use of only etoposide and to make considerable savings. The second objective was to verify the impact of the mechanical pumping action on the etoposide solutions. This investigation was performed at day 61, at the end of the study.

MATERIALS AND METHOD

Chemicals and reagents

All solvents were of high-performance liquid chromatography (HPLC) grade from VWR Chemicals (VWR Prolabo, Fontenay sous-Bois, France) or Merck Sigma. Formic acid (batch: 151140502), triethylamine (batch: 14J280506) and acetonitrile (batch: 17F211398) were used for the mobile phase. Hydrochloric acid 1M (batch: 16090003) and 0.1M (batch: 171101), sodium hydroxide 1M (Merck; batch HC61977) and 0.1M (batch 170808) and hydrogen peroxide 30% (Merck; lot no. K487438107B) were used for the forced degradation. Water for chromatography was obtained from a reverse osmosis system (Millipore Iberica, Madrid, Spain). Etoposide 20 mg/mL, Concentrate for Solution for Infusion (Etoposide Mylan, batch 2049), Easyflex 0.9% NaCl (MacoPharma, batch 17I01B) or 5% glucose 250 mL (MacoPharma, batch 17E30C) were used for test solutions.

Preparation of test solutions

All manipulations were performed inside a biological safety cabinet.

Stability study in polyolefin bags: for the preparation of the mean concentration 0.4 mg/mL, 0.8 mg/mL, 1.4 mg/mL and 2.0 mg/mL, respectively 5 mL, 10 mL, 17.5 mL and 25 mL of etoposide 20 mg/mL were injected. Two bags were prepared for each concentration, each solvent and each temperature.

The bags are overfilled compared with the theoretical volume of 250 mL. The overfilling of bags depends on the batches used. It was measured in our laboratory by emptying three bags into a graduated cylinder and by calculating the average value. In this stability study, the exact volume of the bags was 259 mL for 0.9% NaCl and 260 mL for 5% glucose bags. The overfilled volume was not removed in this stability study because of the addition of reconstituted etoposide solution. With this overfilling and with the volume of etoposide injected, the theoretical concentrations of etoposide studied are 0.38 mg/mL, 0.74 mg/mL, 1.26 mg/mL and 1.75 mg/mL in 0.9% NaCl and in 5% glucose.

The diluted test solutions in infusions bags were stored under refrigeration (2°C to 8°C) and at 25°C in a climatic chamber, protected from light.

HPLC assay

Etoposide concentrations were analysed by a stability-indicating reversed-phase high-performance liquid chromatography (RP-HPLC) method with photodiode array detection adapted from European pharmacopoeia.¹¹

The HPLC system consisted of an ELITE LaChrom VWR/Hitachi plus autosampler, a VWR photodiode array (PDA) detector L-2455 and a VWR L-2130 HPLC-pump. Data was acquired and integrated by using EZChrom Elite (VWR, Agilent). The column used was LiChrospher 100 RP-18, LiChro-CART 125-4, length 12.5 cm and particle size 5 µm (Analytical Chromatography, Merck) with a gradient from formic acid (VWR, France), triethylamine (VWR, France) and ultrapure water (solution A) to formic acid, triethylamine and acetonitrile (acetonitrile HPLC gradient grade (VWR, France)) (solution B). The gradient was set up as follows: start (0 min), 75% A; 25% B; 12 min: 27% A; 73% B.

The flow rate was set at 1 mL/minute, with an injection volume of 50 µL. The detection wavelength was set at 285 nm. The temperature of the injector was set at 23°C and the temperature of the column at 40°C. Under these conditions, the retention time of etoposide was around 9.5 min. The calibration curve was constructed from plots of peak area versus concentration. The linearity of the method was evaluated for five concentrations (10, 30, 50, 70, 90 µg/mL).

One millilitre of etoposide 20 mg/mL was diluted in 0.9% NaCl 200 mL. This solution was used to prepare standard curves by diluting with 0.9% NaCl. The intraday and interday precisions were evaluated at 50 µg/mL. The intra-day reproducibility was evaluated as recommended by ICH Q2 (R1),¹² using six determinations at 100% of the test concentration: 50 µg/mL. For interday precision, six injections of etoposide at 50 µg/mL were assayed daily on three consecutive days. To demonstrate the specificity of the method and the absence of interaction between etoposide and its excipients, a solution for each excipient of etoposide (polysorbate 80, polyethylene glycol 300, benzyl alcohol, citric acid) was realised and analysed by HPLC.

The stability-indicating capability was evaluated by analysing forced degraded etoposide solutions.

Acidic conditions: a solution of 200 µg/mL etoposide 1 mL was diluted with 1 mL HCl 0.5M, stored at 25°C for 15 min, neutralised by 1 mL of NaOH 0.5M and diluted with 1 mL of 0.9% NaCl to obtain a theoretical concentration of 50 µg/mL.

Alkali degradation: a solution of 200 µg/mL etoposide 1 mL was diluted with 1 mL NaOH 0.01M, stored at 25°C for 5 min, neutralised by 1 mL of HCl 0.01M and diluted with 1 mL of 0.9% NaCl to obtain a theoretical concentration of 50 µg/mL.

Oxidative degradation: a solution of 200 µg/mL etoposide 1 mL was diluted with H₂O₂ 3% 1 mL stored at 25°C and diluted with 2 mL of 0.9% NaCl to obtain a theoretical concentration of 50 µg/mL.

UV degradation: a solution of 50 µg/mL etoposide was exposed for 15 min, 30 min, 1 hour and 12 hours under a sun-like spectrum lamp at 254 nm (Vilbert Lourmat).

Heat degradation: a solution of 50 µg/mL etoposide was exposed to a temperature of 60°C for 15 min, 30 min, 1 hour and 12 hours.

Sample dilution for analysis by RP-HPLC

The solutions were diluted before analysis with 0.9% NaCl or 5% glucose to obtain approximately 50 µg/mL concentration (middle of the standard curve).

An etoposide solution at 0.38 mg/mL: 1 mL was diluted with 7 mL of 0.9% NaCl or 5% glucose. An etoposide solution at 0.74 mg/mL: 0.5 mL was diluted with 7.5 mL of 0.9% NaCl or 5% glucose. An etoposide solution at 1.26 mg/mL in 0.9% NaCl and in 5% glucose: 0.25 mL was diluted with 6.75 mL of 0.9% NaCl or 5% glucose. An etoposide solution at 1.75 mg/mL in 0.9% NaCl and in 5% glucose: 0.25 mL was diluted with 9.75 mL of 0.9% NaCl or 5% glucose.

The diluted solutions were analysed after preparation and after 9, 16, 21, 28 and 61 days. After dilution, the samples were analysed by RP-HPLC.

Total run time was set at 40 min. A single sample was taken from each bag each day of the assay.

Chemical stability was defined as not less than 95% of the initial etoposide concentration.¹³

pH measurement

pH measurement was performed using a Crison pH25 pH-meter. Analysis was carried out for each concentration, each solvent and each temperature after preparation and on days 9, 16, 21, 28 and 61 days. pH values were considered to be acceptable if they did not vary by more than 1 pH unit from the initial measurement. We measured pH only on one bag for each condition.

Determination of physical stability

Physical stability was realised with a visual examination: colour changes and particulate matter every day of the assay. The subvisual evaluation was assessed by using a Safas Monaco UV mc2 spectrophotometer. After using an infusion pump, we measured the effect on turbidity by UV spectrophotometry. During the study, we measured turbidity only on one bag for each condition. The absorbance light was scanned at 550 nm. The absorbance of more than 0.010 AU was considered as evidence of turbidity, providing a quantitative determination of incompatibility.¹⁴ An absorbance reading less than 0.010 AU was considered to be a noise level.

Influence of an infusion pump

On day 61, we studied the effect of mechanical action on the physical stability of etoposide solutions with an infusion pump.

One bag for each condition was analysed by RP-HPLC and with a visual examination, after the action of an infusion volumetric pump (Volumat Agilia, Fresenius Kabi):

- Each solvent: NaCl 0.9% or 5% glucose.
- Each temperature: 25°C or 2°C–8°C.
- Each concentration: 0.38, 0.74, 1.26 and 1.75 mg/mL.

Bags which have precipitated before day 61 cannot be analysed. A Volumat administration set including an in-line 0.2 µm micro-filter was attached on each bag physically stable on day 61. The content of the etoposide bag was emptied into an empty bag during 15 to 20 min. We studied the effect of the infusion pump only on one bag for each condition.

RESULTS

Reversed phase HPLC

The calibration curve was linear, the correlation coefficient was 0.99998. The equation of the calibration curve was $y = 81158.17833x - 12234.183$. The intra-day precision expressed as relative standard deviation (RSD) was 1.01%. The inter-day precision expressed as relative standard deviation (RSD) was 2.25%. The absence of interference by excipients was validated.

Stability indicating capacity was proved by using various stressed conditions. The retention time of etoposide was 9.7 min. Chromatogram obtained after alkaline stressed conditions is presented in figure 1 for example.

The mass balance was evaluated and is presented in table 1. Area for exclusion limit was established at 2020.

Chemical stability of solutions

HPLC assay

The percentage of etoposide diluted in 0.9% NaCl after storage at 25°C and at 2°C to 8°C for various time points is shown in table 2. The percentage of etoposide diluted in 5% glucose after storage at 25°C and at 2°C to 8°C for various time points is shown in table 3.

For etoposide diluted in 0.9% NaCl at 25°C, we observed a degradation product. The evolution of this main degradation product expressed as the percentage of surface area of total products on the chromatogram is presented in figure 2. It was not observed at 2°C to 8°C and minor in 5% glucose (<1%).

Figure 1 Chromatogram of etoposide after alkaline stressed conditions.

Table 1 Mass balance of etoposide solutions after various stressed degradations

Peaks	Retention time (min)	Relative retention	Area		
			Without stressed degradation	HCl 0.5M 15 min	NaOH 0.01M 5 min
1	2.2	0.23		2748	
3	2.6	0.27		22 167	
4	3	0.31		10 313	
5	4.1	0.42		22 391	77 588
6	4.4	0.45		282 109	313 681
7	6.5	0.67		8075	
8	7.6	0.78		10 537	8272
Etoposide	9.7	1	4 151 813	3 237 978	2 391 233
10	11.9	1.23		491 595	1 568 659
11	38.1	3.93	64 887	84 555	
Total mass balance			4 216 700	4 172 468	4 359 433
% degradation				22%	42%

pH measurements

All samples diluted in 0.9% NaCl had a pH in the range of 3.32 to 3.97 and in the range of 3.36 to 3.87 in 5% glucose during the study. No significant modification of pH was observed during the whole stability study. For all solutions, the maximum variation obtained between the day of assay and day 0 was 0.15 pH unit.

Physical stability of solutions

Visual aspect

An extensive white precipitate was observed as shown in [figure 3](#) in different solutions (see [tables 2 and 3](#)).

Subvisual evaluation

Concerning turbidity assays, no change was observed except on day 16 for storage between 2°C to 8°C in 5% glucose at 1.75 mg/mL. In other conditions, day of assay and mixture, mean values of absorbance remained inferior to 0.010 AU. On day 16 for 1.75 mg/mL etoposide solution diluted in 5% glucose, stored

between 2°C to 8°C, we observed an absorbance at 0.2367 AU. On day 21, we observed a white precipitate in this bag that was absent on day 16. After the effect of an infusion pump in etoposide solutions, we realised assays by spectrophotometry: no modifications were demonstrated; mean value of absorbance remained inferior to 0.010 AU.

Influence of an infusion pump

Infusion volumetric pumps did not cause:

- ▶ Visual instability such as precipitations.
- ▶ Subvisual instability: absorbance remained inferior to 0.010 AU.
- ▶ Chemical instability on etoposide solutions analysed: percentage consistent with those obtained on day 61.

As seen in [tables 2 and 3](#), some bags have precipitated before day 61 and cannot be analysed for this part: solutions at 1.75 mg/mL diluted in 0.9% NaCl and 5% glucose, stored between 2°C

Table 2 Stability of etoposide diluted with 0.9% sodium chloride at 25°C and 2°C to 8°C

Theoretical concentration (mg/mL)	% initial concentration remaining				
	9 days	16 days	21 days	28 days	61 days
25°C					
0.38	93.10%	97.54%	98.77%	97.08%	91.77%
0.38	95.12%	96.80%	96.91%	97.46%	97.14%
0.74	95.84%	96.27%	95.84%	93.70%	P
0.74	94.64%	97.99%	93.80%	95.76%	P
1.26	95.11%	97.00%	98.24%	98.08%	93.06%
1.26	89.39%	94.65%	94.36%	95.26%	91.62%
1.75	97.80%	96.23%	95.23%	97.90%	93.00%
1.75	93.68%	95.59%	92.59%	93.19%	P
2–8°C					
0.38	99.83%	98.78%	98.65%	99.86%	102.74%
0.38	98.53%	97.27%	98.40%	99.40%	98.46%
0.74	95.17%	100.87%	98.99%	101.80%	P
0.74	103.76%	100.75%	103.51%	105.44%	107.71%
1.26	95.11%	97.09%	98.27%	P	–
1.26	95.11%	98.38%	100.25%	99.97%	P
1.75	102.75%	P	–	–	–
1.75	P	–	–	–	–

Note, Drug concentrations in samples taken at time zero were designated as 100%. P=precipitations.

Table 3 Stability of etoposide diluted with 5% glucose at 25°C and 2°C to 8°C

Theoretical concentration (mg/mL)	% initial concentration remaining			
	9 days	21 days	28 days	61 days
25°C				
0.38	97.56%	95.84%	96.97%	98.72%
0.38	100.58%	99.65%	101.23%	101.89%
0.74	99.73%	97.18%	98.53%	95.15%
0.74	96.04%	96.93%	95.07%	94.79%
1.26	98.37%	98.79%	96.80%	101.71%
1.26	98.18%	97.30%	99.42%	97.89%
1.75	99.92%	98.82%	98.89%	P
1.75	98.67%	98.34%	95.09%	94.21%
2–8°C				
0.38	93.78%	99.46%	99.88%	P
0.38	99.93%	102.58%	100.41%	104.07%
0.74	98.17%	99.35%	99.58%	P
0.74	97.69%	100.99%	98.86%	103.78%
1.26	91.87%	99.31%	98.08%	105.31%
1.26	94.83%	99.85%	99.01%	105.34%
1.75	96.67%	99.53%	99.33%	P
1.75	97.87%	P	–	–

Note, Drug concentrations in samples taken at time zero were designated as 100%. P=precipitations.

to 8°C, solutions at 1.26 mg/mL in 0.9% NaCl, stored between 2°C to 8°C and at 0.74 mg/mL in 0.9% NaCl, stored at 25°C.

DISCUSSION

Stability in 5% glucose

Diluted in 5% glucose and stored at 25°C, etoposide solutions at 0.38, 0.74 and 1.26 mg/mL retained more than 95% of the initial concentration for 61 days. At 1.75 mg/mL, etoposide solutions were stable for 28 days. Under these conditions, no degradation products were observed. No significant change of pH was observed. No precipitate was observed and turbidimetry was not modified. These data can be used in daily practice for long-term advance preparation and high etoposide concentrations.

Our results are in accordance with Sadou Yaye et al. They determined a stability of 21 days for etoposide solutions at 0.4 and 0.6 mg/mL in 5% glucose at room temperature.¹⁵

Diluted in 5% glucose and stored at 2°C to 8°C, etoposide solutions at 0.38, 0.74 and 1.26 mg/mL retained more than 95% of the initial concentration for 28 days. Etoposide diluted at 1.75 mg/mL in 5% glucose and 0.9% sodium and stored in a refrigerator is not recommended.

Stability in 0.9% NaCl

Diluted in 0.9% NaCl and stored at 25°C, etoposide solutions at 0.38, 0.74, 1.26 and 1.75 mg/mL retained more than 95% of the initial concentration for 16 days. One bag at 1.26 mg/mL has less than 90% of the initial etoposide concentration on day 9. A homogenisation problem can justify this value. If we compare with the other solution prepared in the same conditions: on day 9, this sample retained more than 95%. The main degradation product (MDP), with relative retention at 0.27, gradually increased during the study, up to approximately 10% on day

Figure 2 Evolution of the main degradation product with a retention time of 2.6 min expressed as the percentage of all peaks in etoposide solutions in 0.9% NaCl stored at 25°C.

Figure 3 The precipitated etoposide solution, stored at 2°C to 8°C.

61 for an etoposide solution diluted in 0.9% NaCl at 1.75 mg/mL and stored at 25°C. This peak does not correspond to impurities identified by European pharmacopoeia.¹¹ This peak was observed after acidic forced degradation of etoposide solutions (table 1). Solvent 0.9% NaCl has a pH at 6 to 6.5 but etoposide solutions diluted in 0.9% NaCl have acidic pH between 3.32 to 3.97 and can explain the formation of this degradation product. This peak is equally present in etoposide solutions diluted in 5% glucose, but less than 2% and constant during the stability study. This is one reason for limiting the duration of the stability of an etoposide solution diluted in 0.9% NaCl and stored at 25°C for 16 days. The second reason is that several etoposide solutions diluted in 0.9% NaCl retained less than 95% of the initial concentration.

Sadou Yaye et al determined 21 days of stability for etoposide solutions at 0.4 and 0.6 mg/mL in 0.9% NaCl at room temperature.¹⁵

Diluted in 0.9% NaCl and stored between 2°C to 8°C, etoposide solutions at 0.38 and 0.74 retained more than 95% of the initial concentration for 28 days. One solution at 0.74 mg/mL diluted in sodium chloride, between 2°C to 8°C, obtained more than 100% of the initial concentration on days 9, 16, 21 and 28. That can be explained by a low initial concentration on day 0 due to a homogenisation problem compared with the value for the other bag with the same conditions.

Total run time was 40 min. This duration limited us on the replicate analysed. In fact, we analysed only one sample for each preparation each day of the analysis. RSD% could not be calculated.

With 0.9% NaCl as solvent, the precipitation at 2°C to 8°C for higher concentrations was faster than in 5% glucose.

The effect of pump infusion with an administration set including an in-line micro-filter on solutions did not cause any modifications on etoposide solutions.

CONCLUSION

Etoposide diluted in 5% glucose at 0.38, 0.74 and 1.26 were stable over 61 days at 25°C. Etoposide solutions diluted in 5% glucose 1.75 mg/mL were stable 28 days at 25°C.

These results allow advanced preparation, minimise drug wastage, overcomes Etopophos shortages, make considerable

savings and prepare etoposide solutions with higher concentrations for patients with fluids restriction or high doses of etoposide.

The storage between 2°C to 8°C and high concentrations of etoposide favour precipitation. We can observe that precipitation solutions are variable and are not constant under all conditions. We recommended using an administration set with an in-line micro-filter. The action of infusion volumetric pumps has not caused solution precipitations.

Key messages

What is already known on this subject

- The diluted solution of etoposide should not exceed 0.4 mg/mL because precipitation may occur.

What this study adds

- New stability data for etoposide: 28 days of stability for etoposide solution diluted in 5% glucose at 1.75 mg/mL, stored at room temperature.
- The action of infusion volumetric pumps has not caused solution precipitations.
- Possibility to use an administration set with an in-line micro-filter

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