IV Compatibility Product

Trissel's Drugs and Solutions Data

Ifosfamide

Trade Name(s)	IFEX;IFEX NOVAPLUS
Other Name(s)	Isoendoxan;Isophosphamide;Iphosphamide
pH Range [1408]	Approximately pH 6
Formulation [1017]	Provided as a dry white powder in vials containing ifosfamide 1 g and 3 g in packages also containing mesna injection.
Reconstitution [1017] [1018] [1274] [1931] [1932]	Ifosfamide is cited by NIOSH as a drug that should be handled as hazardous. Reconstitute the 1 g and 3 g vials with 20 mL or 60 mL, respectively, of sterile water for injection or bacteriostatic water for injection resulting in a clear, colorless 50-mg/mL solution. Ifosfamide should be diluted to a concentration between 0.6 and 20 mg/mL for administration. Density: The density of ifosfamide at a concentration of 50 mg/mL in sterile water for injection was determined to be 1.01 g/mL. The density may be used for quality assurance of the accuracy of the drug volume added to infusion solutions.
Storage [1017] [1408]	Store intact containers of ifosfamide at controlled room temperature and protect from exposure to excessive heat. Ifosfamide will liquefy at temperatures exceeding 35 °C.
Maximum Stability [2229] [2814] [2816] [1408]	Maximum reported stability periods: Reconstituted solution- 7 days at room temperature and 6 weeks refrigerated. In D5W- 8 days at room temperature and 6 weeks refrigerated. In NS- 31 days at room temperature and 6 weeks refrigerated.
Stability (Detailed) [2812] [2653] [2813] [2229] [1017] [1018] [2814] [1838] [2811] [2815] [1408] [1026]	Ifosfamide in intact vials stored as directed by the manufacturer is stable until the labeled expiration date. Martel et al. reported that the stability of ifosfamide in intact vials stored at an elevated temperature of 33 °C protected from exposure to light for 12 months exhibited little or no loss of drug when tested by stability-indicating HPLC analysis. The authors stated such temperatures might be reached during transportation of the vials during summer months. Behme et al. reported that ifosfamide reconstituted with benzyl alcohol-preserved bacteriostatic water for injection developed turbidity and separated into 2 phases. Dilution to a concentration of 60 mg/mL or less resulted in the phases dissolving completely, and no loss of ifosfamide or the preservative.

Trissel et al. reported that reconstituted ifosfamide is physically and chemically stable for 7 days at room temperature and up to 6 weeks refrigerated. The manufacturer indicates the reconstituted solution should be stored under refrigeration and discarded after 24 hours.

Radford et al. reported the stability of ifosfamide 80 mg/mL in sodium chloride 0.9% at body temperature of 37 °C protected from exposure to light. HPLC analysis found about 7% loss occurred in 9 days.

Infusion Solutions:

Ifosfamide 0.6 to 20 mg/mL is physically compatible and stable for at least 7 days at room temperature and 6 weeks refrigerated in the following infusion solutions:

Dextrose 2.5% and 5%

Dextrose 2.5% in sodium chloride 0.45%

Dextrose 5% in sodium chloride 0.45%

Dextrose 5% in sodium chloride 0.9%

Lactated Ringer's injection

Sodium chloride 0.9%

Ostermann-Kraljevic et al. reported the stability of ifosfamide 3 and 16 mg/mL in dextrose 5% and sodium chloride 0.9% in glass and polyethylene containers. The solutions were physically stable, and HPLC analysis found no loss of ifosfamide with 8 days at room temperature of 22 to 24 °C.

Dine et al. reported that ifosfamide 30 mg/mL in both dextrose 5% and in sodium chloride 0.9% in polyvinyl chloride (PVC) plastic bags loss less than 10% of the drug concentration in 30 days stored refrigerated at 4 °C and protected from exposure to light.

Cabanas Poy et al. have indicated the possibility of even longer stability periods in dextrose 5% in sodium chloride 0.9% and also sodium chloride 0.9% in glass, polyvinyl chloride (PVC), and polypropylene containers at ambient temperature.

Cabanas et al. calculated the time to 10% drug loss (t90) of ifosfamide in sodium chloride 0.9% and in dextrose 5% in sodium chloride 0.9%. Using HPLC analysis, ifosfamide was found to be very stable in sodium chloride 0.9% with 10% loss occurring in 31 to 36 days. The stability in dextrose 5% in sodium chloride 0.9% was good but decreased. The time to 10% drug loss was as little as 13 days.

Packaged in Syringes:

Bristol Myers Oncology indicates that ifosfamide 0.6 to 20 mg/mL in dextrose 5%, sodium chloride 0.9%, lactated Ringer's injection, and sterile water for injection packaged in Becton Dickinson polypropylene syringes is physically and chemically stable for 24 hours at room temperature.

pH Effects [2807] [2808] [2809] [2810] [2811]

Ifosfamide is stable over the pH range of 4 to 10 exhibiting a similar rate of decomposition throughout the pH range. Above pH 10 and below pH 4, increased decomposition occurs.

Ifosfamide and mesna are stable in admixtures together exhibiting stability for up to 9 days at room temperature and 14 days refrigerated. However, Saito et al. reported that if the solution is made slightly alkaline by the addition of sodium bicarbonate, mesna is much less stable. In solutions

	having a pH of 8, HPLC analysis found that mesna was stable for about 6 hours, but lost 13% in 24 hours and 23% in 48 hours. Ifosfamide lost 6% in 24 hours and 14% in 48 hours.
Interaction with Plastics [2653] [2813] [2229] [2814] [2808] [2816] [1838] [2817] [1408]	Ifosfamide has not been found to undergo substantial sorption to polyvinyl chloride (PVC) containers, PVC infusion set tubing, polyethylene containers, polypropylene (in syringes), or glass containers.
Other Information [1936] [2818] [1274]	Ifosfamide is cited by NIOSH as a drug that should be handled as hazardous. Microbial Growth Potential: Paris et al. reported that B. subtilis and C. albicans exhibited viability in reconstituted ifosfamide solution. Quality Control: Lelievre et al. described an approach to quality control and accuracy assessment for 22 cancer chemotherapy drugs, including ifosfamide, which is designed to reduce the risk of erroneously prepared doses reaching patients. The technique utilized an ultraviolet (UV)-visible and infrared (IR) scanning analysis (Multispec, Microdom) of the finished dosage forms to verify the right molecule, concentration, and solution. Of 3149 doses of the 22 drugs tested, 7.82% varied by more than 10% from the intended concentration.
pHmax	6
pHmean	6
pHmin	6

Reference Section