CEFAZOLIN SODIUM (cont'd-1)

Issued 12/97

Stability of Cefazolin Sodium Reconstituted for IM Use:

		% of original	
		RT 24 hrs	5°C 96 hrs
Sterile Water	1 g	96	97
for Injection	500 mg	98	98
Bacteriostatic	1 g	100	100
Water for Injn. (benzyl alc)	500 mg	100	100
Bacteriostatic Water for Injn. (parabens)	500 mg	100	100
Sodium Chloride	1 g	91	100
Injection #, ##	500 mg	93	100
Bacteriostatic Sodium Chloride Solution (Benzyl alc)	500 mg	100	102

#When 1 g Kefzol or Ancef are reconstituted with 2.5 ml 0.9% sodium chloride, heavy crystal formation may be seen after several hours. Sterile water for injection is recommended but, if NS must be used, the drug should be administered immediately after complete dissolution has occurred (747).

##Because of possibility of crystal formation and as a safety precaution, 0.9% sodium chloride injection has been deleted from FDA-approved product labeling as a recommended diluent for 1 g vials of Ancef or Kefzol for intramuscular use (794).

One g cefazolin, reconstituted with 2.5 ml water, physically compatible with one liter of:

Normosol-M in D5W
Plasmalyte 56 in 5% Dextrose
5% Dextrose Injection with Vitamins
5% Dextrose and 0.9% NaCl Injection
5% Dextrose in Lactate Ringer's Injn
0% Dextrose and 0.9% NaCl InjCTN.

Concomitant administration of cefazolin sodium and other antibiotics in same syringe or IV bottle not recommended by manufacturer (166).

Cefazolin was stable in peritoneal dialysis solutions containing 1.5% and 4.24% dextrose for 14 days at 4°C, 8 days at 25°C, and 24 hours at 37°C (1181).

Preparation and Administration (234)

INTRAMUSCULAR ADMINISTRATION — Reconstitute with Sterile Water for Injection, Bacteriostatic Water for Injection or Sodium Chloride Injection#, according to following dilution table:

Vial Size	Diluent to be added	Approx. avail. volume	Approx avg. conc.
250 mg	2.0 ml	2.0 ml	125 mg/ml
500 mg	2.0 ml	2.2 ml	225 mg/ml
1 g	2.5 ml	3.0 ml	330 mg/ml

Shake until dissolved and inject into a large muscle mass.
#When 1 g Kefzol or Ancef are reconstituted with 2.5 ml 0.9% sodium chloride, heavy crystal formation may be seen after several hours. Sterile water for injection is recommended but, if NS must be used, the drug should be administered immediately after complete dissolution has occurred (747).

INTRAVENOUS ADMINISTRATION — Cefazolin may be administered by intermittent or continuous infusion or by direct IV injection. For intermittent IV infusion, cefazolin can be administered in a volume control set or in a separate, secondary IV bottle. Reconstituted 500 mg or 1 g of cefazolin may be diluted in 50 ml to 100 ml of one of the following intravenous solutions:

Sodium Chloride Injection
5% or 10% Dextrose Injection
5% Dextrose in LR Injn.
5% Dextrose and 0.9% Sodium Chlor.
Lactated Ringer's Injection
Invert Sugar 5% or 10% in Water
Ringer's Injection
5% Sodium Bicarbonate in Water
5% Dextrose and 0.45% or 0.2% Sodium Chloride Injn.

Ancef is stable in these intravenous fluids for 24 hours at room temperature and 96 hours under refrigeration (613).

For direct intravenous injection, dilute the reconstituted 500 mg or 1 g of cefazolin in a minimum of 10 ml of Sterile Water for Injection. Inject solution slowly over 3 to 5 minutes. May be administered directly into vein or through tubing for patient receiving the above parenteral fluids (234). Solutions of cefazolin, 20 mg/ml or 50 mg/ml in D5W, have osmolalities of approximately 325 and 412 mOsm/kg, respectively. The same concentrations in NS have osmolalities of approximately 347 and 426 mOsm/kg, respectively (1110a).

CEFAZOLIN SODIUM (cont'd-2)

Issued 3/78

The package literature for cefazolin sodium recommends that solutions be discarded after 24-hour storage at room temperature or 96 hours storage at 5°C. This specific recommendation is made to minimize the potential for growth of microorganisms inadvertently introduced during reconstitution and subsequent manipulation of the antibiotic solution. Other factors that make the shorter storage period the one of choice are an increase in color and a change in pH (189, 190)

Table 1. Cefazolin Sodium Microbiological Solution Stability

		% Initial Cefazolin Activity									
		5ºC			25ºC					37ºC	
Diluent	**Concentration**	**4 Days**	**7 Days**	**14 Days**	**1 Day**	**2 Days**	**4 Days**	**7 Days**	**14 Days**	**4 Days**	**7 Days**
Water for injection	1 g/4 ml	97.5	97.4	97.4	96.6	90.7	91.6	84.9	63	75.2	46.2
Water for injection	1 g/3 ml	100.8	——	——	99.2	——	95.4	——	——	——	——
Water for injection	500 mg/2 ml	97.9	——	——	92.2	——	97.4	——	——	——	——
Water for injection	250 mg/2 ml	86.4	——	——	94	——	80.9	——	——	——	——
Water for injection	500 mg/100 ml	108.5	——	102.9	99	93.8	100	——	90	79.8	64.2
0.9% sodium chloride	500 mg/100 ml	101.3	95.6	86.7	100	100	100	94.3	85.2	83	63.8
Dextrose 5% in water	500 mg/100 ml	101.1	93.2	95.8	96.7	95.7	93.6	89.7	79.7	79.5	66.2
D5W with 0.02% NaHCO3	500 mg/100 ml	——	94.4	95.5	100.3	95.1	——	88.5	85.2	80.9	51.6
D5W in lactated Ringer's	500 mg/100 ml	100.5	99.6	96.4	101.4	97.9	92.5	90.4	80.7	79.2	67.9
Lactated Ringer's injection	500 mg/100 ml	——	99.1	101.6	102.2	100	——	91.3	80.4	88	62.7
Normosol-M in D5W	500 mg/100 ml	101.3	98.5	96.6	97.9	98.3	98.8	92.4	80.8	77.3	67.4
Ionosol B in D5W	500 mg/100 ml	102	103.4	98.3	102.8	96.6	99.6	92.1	80.5	77.9	67.1
Plasmalyte in D5W	500 mg/100 ml	——	100.1	102.6	102.1	98.3	——	93.7	90.5	85.6	61.5

Table 2. Cefazolin Sodium Polargraphic Solution Stability

		% Initial Cefazolin Assay				
		25ºC			37ºC	
Diluent	**Concentration**	**2 days**	**4 days**	**14 days**	**4 days**	**7 days**
Water for injection	1 g/4 ml	96.2	89.7	81.2	79.0	68.5
Water for injection	500 mg/100 ml	96.2	95.3	86.6	89.8	80.8
0.9% sodium chloride	500 ml/100 ml	99.5	91.7	89.1	89.5	83.9
Dextrose 5% in water	500 ml/100 ml	99.7	94.1	87.5	85.7	79.0
D5W with 0.02% NaHCO3	500 mg/100 ml	98.2	98.8	88.0	75.0	79.0
D5W in lactated Ringer's	500 mg/100 ml	98.6	95.0	87.4	85.5	75.6
Lactated Ringer's injection	500 mg/100 ml	99.6	98.7	89.0	87.1	79.2
Normosol-M M in D5W	500 mg/100 ml	97.8	95.8	84.2	80.4	70.6
Ionosol B in D5W	500 mg/100 ml	100.0	97.0	87.0	84.0	76.0

Table 3. Cefazolin Sodium pH Solution Stability

		pH							
		5ºC			25ºC			37ºC	
Diluent	**Concentration**	**Init'l.**	**4 days**	**14 days**	**1 day**	**4 days**	**14 days**	**4 days**	**7 days**
Water for injection	1 g/4/ml	5.55	5.51	5.50	5.65	6.33	6.50	6.51	6.53
Water for injection	1g/3 ml	5.60	5.60	——	5.74	6.28	——	——	——
Water for injection	500 mg/2 ml	5.60	5.60	——	6.10	6.34	——	——	——
Water for injection	250 mg/2 ml	5.50	5.56	——	6.10	6.26	——	——	——
Water for injection	500 mg/100 ml	5.37	5.62	5.38	5.69	6.20	5.93	6.33	6.43
0.9% sodium chloride	500 mg/100 ml	5.00	5.66	5.69	5.59	6.10	6.27	6.50	6.70
Dextrose 5% in water	500 mg/100 ml	4.80	5.60	5.65	5.70	6.13	6.33	6.57	6.73
D5W with 0.02% NaHCO3	500 mg/100 ml	7.10	6.60	6.90	6.82	6.73	6.69	6.33	6.40
D5W in lactated Ringer's	500 mg/100 ml	4.75	5.10	5.01	5.02	5.20	5.47	5.72	6.02
Lactated Ringer's injection	500 mg/100 ml	6.21	6.30	6.29	6.10	6.30	6.45	6.31	6.48
Normosol-M in D5W	500 mg/100 ml	5.05	5.09	5.05	5.12	5.10	5.21	5.31	5.42
Ionosol B in D5W	500 mg/100 ml	5.95	5.95	5.99	6.00	5.99	6.00	5.89	6.00
Plasmalyte in D5W	500 mg/100 ml	5.43	5.40	5.40	5.45	5.45	5.49	5.51	5.59

CEFAZOLIN SODIUM (cont'd-3)
Issued 4/78

Table 4. Frozen Solution Stability (Microbiological) of Cefazolin Sodium (332)

	% of initial Cefazolin Activity									
	-10ºC						-20ºC			
Diluent in weeks	**1**	**2**	**4**	**6**	**12**	**26**	**2**	**4**	**6**	**26**
Concentration: 1g with 2.5 ml										
Water for Injection USP	——	103.4	——	100.2	——	101.7	106.3	——	102.6	104.3
Water for Injection USP[a]	——	——	——	98.3	——	101.2	——	——	——	——
0.9% Sodium Chloride Injection USP	——	106.3	——	100.3	——	104.2	103.5	——	98.6	102.6
5% Dextrose Injection USP	——	108.1	——	106.0	——	107.2	101.1	——	96.3	104.3
Concentration: 500 mg with 100 ml										
Water for Injection USP	104.4	99.0	102.5	——	91.7	——	——	——	——	——
0.9% Sodium Chloride Injection USP	102.3	98.1	101.1	——	97.9	——	——	——	——	——
5% Dextrose Injection USP	100.4	96.1[b]	——	94.3[b]	——	95.3[b]	100.5[b]	——	101.4[b]	100.5[b]
D5W with 0.02% NaHCO3	96.6	128.8[c]	87.3[c]	——	——	——	——	——	——	——
D5W in Lactated Ringer's Injn. USP	105.0	101.6	90.7	——	——	——	——	——	——	——
Lactated Ringer's injection USP	101.9	128.9[c]	97.9	——	——	——	——	——	——	
Ionosol B in D5W	98.9	94.5	87.9[c]	——	——	——	——	——	——	——
Normosol-M in D5W	100.9	98.3	100.9	——	——	——	——	——	——	——
Plasmalyte in D5W	103.2	114.3[c]	95.1	——	——	——	——	——	——	
Concentration: 10 g with 45 ml										
Water for Injection USP	——	——	99.0	100.0	——	100.5	——	98.5	97.5	98.0
0.9% Sodium Chloride Injection USP	——	——	100.0	122.1c	——	105.5	——	100.0	128.1[c]	105.0
5% Dextrose Injection USP	——	103.6	100.0	102.0	——	106.1	104.6	100.0	117.3[c]	106.1

[a] Stored in polyvinyl chloride plastic containers.

[b] Turbidimetric assay average of two lots. Accuracy of 26-week turbidimetric data was verified with microbiological plate test results.

[c] Variations in microbial assay values do occur somewhat frequently because of temperature, media, microorganism, etc.

Table 5. Frozen Solution Stability (Polarographic) of Cefazolin Sodium (332)

	% Of Initial Cefazolin Activity					
	-20ºC				-10ºC	
DILUENT (in weeks)	**1**	**2**	**4**	**12**	**6**	**26**
Concentration: 1g with 2.5 ml						
Water for Injection USP[a]	——	——	——	——	96.7	96.0
Concentration: 500 mg with 100 ml						
Water for Injection USP	103.2	100.4	99.1	101.0	——	——
0.9% Sodium Chloride Injection USP	103.4	101.8	103.0	98.6	——	——
5% Dextrose Injection USP	94.1	103.2	102.6	99.6	——	——
D5W with 0.02% NaHCO3	100.0	97.0	95.0	99.0	——	——
D5W in Lactated Ringer's Injection USP	98.2	103.3	101.8	98.5	——	——
Lactated Ringer's injection USP	99.6	97.3	98.6	100.0	——	——
Ionosol B in D5W	102.0	101.0	101.0	100.0	——	——
Normosol-M in D5W	100.6	100.6	98.3	101.0	——	——
Plasmalyte in D5W[b]	98.5	98.8	101.5	——	——	——

[a] Stored in polyvinyl chloride plastic containers, performed by iodometric titration.

[b] Performed by iodometric titration.

CEFAZOLIN SODIUM (cont'd-4)
Issued 3/81

Table 6. Frozen Solution pH of Cefazolin Sodium (332)

		pH										
		-20ºC						-10ºC				
in weeks	Initial	1	2	4	6	12	26	Initial	2	4	6	26
Concentration: 1g with 2.5 ml												
Water for Injection USP	5.90	——	6.20	——	6.40	——	6.20	6.00	6.20	——	6.50	6.30
Water for Injection USP[a]	5.30	——	——	——	5.64	——	5.42	——	——	——	——	——
0.9% Sodium Chloride Injn USP	5.80	——	6.20	——	6.20	——	6.10	5.70	6.00	——	6.40	6.30
5% Dextrose Injection USP	5.70	——	6.20	——	6.40	——	6.10	5.40	6.20	——	6.40	6.30
Concentration: 500 mg with 100 ml												
Water for Injection USP	5.47	5.32	5.34	5.60	——	5.31	——		——	——	——	——
0.9% Sodium Chloride Injn USP	4.81	5.35	5.30	5.15	——	5.38	——		——	——	——	——
5% Dextrose Injection USP	5.36[b]	5.50	4.99[b]	5.03	4.80[c]	5.60	——	5.50[c]	5.10[c]	——	4.85[c]	5.05[c]
D5W with 0.02% NaHCO3	7.10	7.02	7.00	7.12	——	6.81	——		——	——	——	——
D5W in Lactated Ringer's USP	4.75	5.04	5.00	4.92	——	4.95	——		——	——	——	——
Lactated Ringer's injection USP	6.21	6.01	6.51	6.43	——	6.59	——		——	——	——	
Ionosol B in D5W	5.95	5.95	5.93	5.97	——	5.99	——		——	——	——	——
Normosol-M in D5W	5.05	5.03	5.05	5.02	——	5.00	——		——	——	——	——
Plasmalyte in D5W	5.43	5.40	5.40	5.42	——	5.43	——		——	——	——	——
Concentration: 10 g with 45 ml												
Water for Injection USP	5.50	——	——	6.10	5.70	——	5.90	5.50	——	6.10	5.80	6.00
0.9% Sodium Chloride Injn USP	5.50	——	——	6.00	5.60	——	5.80	5.50	——	6.00	5.70	6.00
5% Dextrose Injection USP	5.50	——	5.70	6.00	5.70	——	5.80	5.50	5.80	6.10	5.80	6.00

a Stored in polyvinyl chloride plastic containers.
b Average of three lots.
c Average of two lots.

Frozen cefazolin solutions thawed in a microwave oven have been show to retain at least 90% of their initial potency. Solution temperatures should not be allowed to exceed 20° and other precautions applicable to microwave oven operation must be observed (458).

Cefazolin, 1 g/3 ml, reconstituted with water, stable for 9 months when frozen at -20° in Hy-Pod syringes (497). When the cefazolin was reconstituted with 0.5% lidocaine injection, the frozen solutions turned cloudy after thawing (497). When solutions of cefazolin were made with 0.5% lidocaine injection and stored in the refrigerator, extensive precipitation was observed within 3 to 4 hours (497).