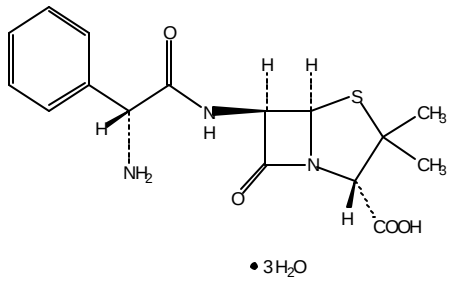
sigma-aldrich.com
3050 Spruce Street, Saint Louis, MO 63103 USA
Tel: (800) 521-8956 (314) 771-5765 Fax: (800) 325-5052 (314) 771-5757
email: techservice@sial.com sigma-aldrich.com

AMPICILLIN
Sigma Prod. No. A6140, A9393, and A9518
Storage Temperature 2-8°C

SYNONYMS: D[-]-a-aminobenzylpenicillin;
6-[D(-)-a-aminophenylacetamido]penicillanic acid (and others[1])

STRUCTURE: Shown for Ampicillin Trihydrate



PHYSICAL DESCRIPTION:

PRODUCT NUMBER	A6140	A9393	A9518
CAS NUMBER	7177-48-2	69-53-4	69-52-3
APPEARANCE	Powder	Powder	Powder
MOLECULAR FORMULA	$C_{16}H_{19}N_3O_4S \cdot 3H_2O$	$C_{16}H_{19}N_3O_4$	$C_{16}H_{18}N_3O_4Na$
MOLECULAR WEIGHT	403.4	349.4	371.4
MELTING RANGE[1,2]	199-202°C	208-222°C	236-239°C
pKa Values	pKa = 2.5 (-COOH) pKa = 7.3 ($-NH_2$) at 25°C[3]	pKa = 2.5 (-COOH) pKa = 7.3 ($-NH_2$) at 25°C[3]	pKa = 2.5 (-COOH) pKa = 7.3 ($-NH_2$) at 25°C[3]
STABILITY AS SUPPLIED[2,4]	non-hygroscopic	hygroscopic	hygroscopic
SOLUBILITY[2]	50 mg/mL in 1 M HCl 10 mg/mL (H_2O)	50 mg/mL in 1 M NH_4OH	50 mg/mL in water

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STABILITY / STORAGE AS SUPPLIED:

A6140 was reported as stable at 25°C at 43% and 81% relative humidity for six weeks, with little change in either moisture content or activity.[5]

SOLUBILITY / SOLUTION STABILITY:

Generally reported as slightly soluble in water, practically insoluble in alcohol, chloroform, ether and fixed oils, but soluble in dilute acids or bases.[3]

A number of studies, including an excellent review article (ref. 5), have indicated that the stability of ampicillin in solution appears to be a function of pH, temperature, and even the identity of the buffer. Although ampicillin in any form is more readily soluble in base, it rapidly loses activity when stored above pH 7.0.[5,6,7] Optimal conditions for storage were suggested as 2-8°C, pH 3.8 to 5, retaining more than 90% activity for a week. Another review noted that the buffer used can also affect stability - at pH 7, Tris is "highly deleterious to the stability...but not so at pH 5...." Citrate is fine at pH 7 but not at pH 5. Acetate buffer seems best at pH 6.[5,6]

Ampicillin in solution is not very stable at pH above 7. Any of the three products can be used, but the pH should be adjusted to 7 or lower for solution stability.

Solution should not be autoclaved; a stock solution of 50 mg/mL should be sterilized by filtration through a 0.22µm filter and stored frozen. Frozen aliquots are expected to be stable for months.[2] This stock can be added to agars or culture media after they have been auto claved and cooled to 45-50°C. A final concentration of 20-60 µg/mL has been recommended. Culture plates with ampicillin can be stored at 2-8°C for up to two weeks before use.[8,9]

GENERAL REMARKS:

Ampicillin is a semi-synthetic derivative of penicillin, active as a broad-spectrum antibiotic. Its spectrum of action is broader than that of benzylpenicillin, especially against gram-negative bacilli. It is inactivated by beta lactamases and for this reason is often administered with a beta lactamase inhibitor. It is similar to benzylpenicillin in its action against gram-positive bacteria; its action is similar to that of the tetracyclines and chloramphenicol against gram-negative bacteria. Minimum inhibitory concentrations for gram-positive organisms have been reported to range from 0.02 to 1.5 µg/mL and for gram-negative organisms from 0.03 to 3 µg/mL.[3]

REFERENCES:

1. *Merck Index*, 12th Ed., #628 (1996).
2. Sigma data.
3. *Martindale: The Extra Pharmacopoeia*, 30th Ed., 116-118; p. xxi (1993).
4. Supplier information.
5. *Analytical Profiles of Drug Substances*, K. Florey, ed., (Academic Press, NY) Vol. 2, 1-61 (1973).
6. Gallelli, *Amer. J. Hosp. Pharm.*, 24, 425-433 (1967)."Stability studies of drugs used in intravenous solutions, part one."
7. Lynn, B., *Brit. J. Intravenous Therapy*, 2, 22 (1981). "The stability and administration of intravenous penicillins."
8. *Molecular Cloning: A Laboratory Manual*, 2nd ed., Sambrook, Fritsch and Maniatis, p. A.6 (and 1.6) (1989).

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Bundgaard, H., *J. Pharm. Pharmac.*, 26, 385-392 (1974). "Spectrophotometric determination of ampicillin sodium..."

Clarke's Isolation and Identification of Drugs, 2nd Ed., Moffat, A.C., ed., Pharmaceutical Press, London, (1986), p. 351. (Analytical data and references for detection in plasma or urine).