

Impurity Table 1

NAME	RELATIVE RETENTION TIME	ACCEPTANCE CRITERIA, NMT (%)
Amoxicillin related compound I ^a (D-hydroxyphenylglycine)	0.32	1.0
Amoxicillin related compound D ^{b,c} (amoxicillin open ring)	0.53	1.0
	0.68	1.0
Amoxicillin related compound A ^d (6-aminopenicillanic acid)	0.78	0.5
Amoxicillin related compound B ^{e,f} (L-amoxicillin)	0.87	—
Amoxicillin	1.0	—
Amoxicillin related compound G ^g (D-hydroxyphenylglycylamoxicillin)	2.9	1.0
Amoxicillin related compound E ^{h,i} (amoxicillin penilloic derivative)	4.5	1.0
Amoxicillin related compound M ^j (N-(penicillan-6-yl) open ring amoxicillinamide)	6.0	1.0
Amoxicillin related compound F ^{e,k} (phenylpyrazinediol)	6.3	—
Amoxicillin related compound C ^l (amoxicillin rearrangement product)	6.4	1.0
Amoxicillin related compound E ^{h,i} (amoxicillin penilloic derivative)	6.7	1.0
Amoxicillin related compound J ^m (amoxicillin open ring dimer)	8.8	1.0
Amoxicillin related compound L ⁿ (N-(penicillan-6-yl) amoxicillinamide)	9.0	1.0
Any unspecified individual impurity	—	1.0

^a(R)-2-Amino-2-(4-hydroxyphenyl)acetic acid.

^bThe chromatographic system resolves two penilloic acids from each other.

^c(4S)-2-[[[(R)-2-Amino-2-(4-hydroxyphenyl)acetamido](carboxy)methyl]-5,5-dimethylthiazolidine-4-carboxylic acid.

^d(2S,5R,6R)-6-Amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

^eThese compounds are listed for information only and are not to be reported.

^f(2S,5R,6R)-6-[(S)-2-Amino-2-(4-hydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

^g(2S,5R,6R)-6-[(R)-2-[(R)-2-Amino-2-(4-hydroxyphenyl)acetamido]-2-(4-hydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

^hThe chromatographic system resolves two penilloic acids from each other.

ⁱ(4S)-2-[[[(R)-2-Amino-2-(4-hydroxyphenyl)acetamido]methyl]-5,5-dimethylthiazolidine-4-carboxylic acid.

^j(2S,5R,6R)-6-(2-[(R)-2-Amino-2-(4-hydroxyphenyl)acetamido]-2-[(4S)-4-carboxy-5,5-dimethylthiazolidin-2-yl]acetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

^k3-(4-Hydroxyphenyl)pyrazin-2-ol.

^l(4S)-2-[5-(4-Hydroxyphenyl)-3,6-dioxopiperazin-2-yl]-5,5-dimethylthiazolidine-4-carboxylic acid.

^m(2S,5R,6R)-6-((2R)-2-[2-[(R)-2-Amino-2-(4-hydroxyphenyl)acetamido]-2-[(4S)-4-carboxy-5,5-dimethylthiazolidin-2-yl]acetamido]-2-(4-hydroxyphenyl)acetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

ⁿ(2S,5R,6R)-6-((2S,5R,6R)-6-[(R)-2-Amino-2-(4-hydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

Acceptance criteria

(Note—The reporting limit is 0.03% of the amoxicillin peak from the *Standard solution*.)

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 5.0%

Specific Tests

- *Crystallinity* (695): Meets the requirements
- *Dimethylaniline* (223): Meets the requirement
- pH (791): 3.5–6.0
Sample solution: 2 mg/mL
- *Water determination, Method I* (921): 11.5% to 14.5%
- *Sterility tests* (71): Where the label states that Amoxicillin is sterile, it meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Direct Inoculation of the Culture Medium*, except to use fluid thioglycollate medium containing polysorbate 80 solution (5 mg/mL) and an amount of sterile penicillinase sufficient to inactivate the amoxicillin in each tube, to use soybean–casein digest medium containing polysorbate 80 solution (5 mg/mL) and an amount of sterile penicillinase sufficient to inactivate the amoxicillin in each tube, and to shake the tubes once daily.
- *Bacterial endotoxins test* (85): Where the label states that Amoxicillin is sterile or Amoxicillin must be subjected to further processing during the preparation

of injectable dosage forms, it contains NMT 0.25 USP Endotoxin Unit/mg of amoxicillin.

Additional Requirements




- *Packaging and storage:* Preserve in tight containers, and store at controlled room temperature.
- *Labeling:* Where it is intended for use in preparing injectable dosage forms, the label states that it is intended for veterinary use only and that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms. Label all other Amoxicillin to indicate that it is to be used in the manufacture of nonparenteral drugs only.
- *USP reference standards* (11)
USP Amoxicillin RS 
USP Amoxicillin Related Compound A RS 
(2S,5R,6R)-6-Amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid; 6-aminopenicillanic acid.
C₈H₁₂N₂O₃S 216.26
USP Amoxicillin Related Compound D RS 
(4S)-2-[[[(R)-2-Amino-2-(4-hydroxyphenyl)acetamido](carboxy)methyl]-5,5-dimethylthiazolidine-4-carboxylic acid; amoxicillin open ring.
C₁₆H₂₁N₅O₆S 383.42
USP Endotoxin RS

FIGURE 1.3 (Continued).