

**CENTER FOR DRUG  
EVALUATION AND  
RESEARCH**

**APPLICATION NUMBER:**

**60-666**

**FINAL PRINTED LABELING**

# BEECHAM

## TOTACILLIN®

### Ampicillin Trihydrate

for  
Oral Suspension

125 mg./5 cc.

and

250 mg./5 cc.

#### Description

TOTACILLIN (Ampicillin Trihydrate) is derived from the penicillin nucleus, 6-aminopenicillanic acid (6-APA), isolated by Beecham. Chemically it is D (-)  $\alpha$ -aminobenzyl penicillin.

#### Actions

##### MICROBIOLOGY:

TOTACILLIN (Ampicillin Trihydrate) is similar to benzyl penicillin in its bactericidal action against sensitive organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide. TOTACILLIN (Ampicillin Trihydrate) differs in *in vitro* spectrum from benzyl penicillin in the Gram negative spectrum: It exerts high *in vitro* activity against many strains of *Hemophilus influenzae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, and *Neisseria catarrhalis*, *Escherichia coli*, *Proteus mirabilis*, *Bacteroides funduliformis*, *Salmonellae* and *Shigellae*.

*In vitro* studies have also demonstrated the sensitivity of many strains of the following Gram positive bacteria: alpha- and beta-hemolytic streptococci, *Diplococcus pneumoniae*, non-penicillinase producing staphylococci, *Bacillus anthracis*, and most strains of enterococci and clostridia. Ampicillin generally provides less *in vitro* activity than penicillin-G against Gram positive bacteria. Because it does not resist destruction by penicillinase it is not effective against penicillinase producing bacteria, particularly resistant staphylococci. All strains of *Pseudomonas* and most strains of *Klebsiella* and *Aerobacter* are resistant.

##### PHARMACOLOGY:

TOTACILLIN (Ampicillin Trihydrate) is acid stable and therefore well absorbed. Food, however, retards absorption. Blood serum levels of approximately 2 mcg./ml. are attained within 1-2 hours following a 250 mg. oral dose given to fasting adults. Detectable amounts persist for about 6 hours. TOTACILLIN (Ampicillin Trihydrate) diffuses readily into all body tissues and fluids with the exception of brain and spinal fluid except when meninges are inflamed. Higher serum levels are obtained following I.M. injection. Most of the ampicillin is excreted unchanged in the urine and this excretion can be delayed by concurrent administration of probenecid. The active form appears in the bile in higher concentrations than found in the serum. TOTACILLIN (Ampicillin Trihydrate) is least serum bound of all the penicillins, averaging about 20% compared to approximately 60%-90% for other penicillins.

#### Indications

TOTACILLIN (Ampicillin Trihydrate) is indicated in the treatment of infections due to susceptible strains of the following:

*Gram Negative Organisms*—*Shigellae*, *Salmonellae* (including *S. typhosa*), *H. influenzae*, *E. coli* and *P. mirabilis*, *N. gonorrhoeae*, and *N. meningitidis*.

*Gram Positive Organisms*—Streptococci, *D. pneumoniae*, and non-penicillinase producing staphylococci.

Because of its wide spectrum and bactericidal action, it may be useful in instituting therapy; however, bacteriological studies to determine the causative organisms and their sensitivity to ampicillin should be performed.

Indicated surgical procedures should be performed.

#### Contraindications

The use of this drug is contraindicated in individuals with a history of an allergic reaction to any of the penicillins.

#### Warnings

SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTOID) REACTIONS HAVE BEEN REPORTED IN PATIENTS ON PENICILLIN THERAPY. ALTHOUGH ANAPHYLAXIS IS MORE FREQUENT FOLLOWING PARENTERAL THERAPY IT HAS OCCURRED IN PATIENTS ON ORAL PENICILLINS. THESE REACTIONS ARE MORE APT TO OCCUR IN INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY AND/OR HYPERSENSITIVITY REACTIONS TO MULTIPLE ALLERGENS. THERE HAVE BEEN REPORTS OF INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY WHO HAVE EXPERIENCED SEVERE REACTIONS WHEN TREATED WITH CEPHALOSPORINS. BEFORE THERAPY WITH A PENICILLIN, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, AND OTHER ALLERGENS. IF AN ALLERGIC REACTION OCCURS, THE DRUG SHOULD BE DISCONTINUED AND THE PATIENT TREATED WITH THE USUAL AGENTS, e.g., PRESSOR AMINES, ANTIHISTAMINES, AND CORTICOSTEROIDS.

#### USAGE IN PREGNANCY:

Safety for use in pregnancy has not been established.

#### Precautions

As with any antibiotic preparation, constant observations for signs of overgrowth of nonsusceptible organisms, including fungi, is essential. Should superinfection occur (usually involving *Aerobacter*, *Pseudo-*

(continued on other side)

(continued from other side)

monas, or Candida), the drug should be discontinued and/or appropriate therapy instituted.

As with any potent agent, it is advisable to check periodically for organ system dysfunction during prolonged therapy: this includes renal, hepatic, and hematopoietic systems. This is particularly important in pretermes, neonates and other infants.

#### Adverse Reactions

As with other penicillins, it may be expected that untoward reactions will be essentially limited to sensitivity phenomena. They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and in those with a history of allergy, asthma, hay fever, or urticaria.

The following adverse reactions have been reported as associated with the use of ampicillin:

**Gastrointestinal**—Glossitis, Stomatitis, black "hairy" tongue, nausea, vomiting, and diarrhea. (These reactions are usually associated with oral dosage forms).

**Hypersensitivity reactions**—skin rashes, urticaria, and erythema multiforme have been reported frequently. A few cases of exfoliative dermatitis have been reported. Anaphylaxis is the most serious reaction experienced and has usually been associated with the parenteral dosage form.

**Note:** Urticaria, other skin rashes, and serum sickness-like reactions may be controlled with antihistamines, and if necessary, systemic corticosteroids. Whenever such reactions occur, ampicillin should be discontinued, unless, in the opinion of the physician, the condition being treated is life threatening and amenable only to ampicillin therapy. Serious anaphylactic reactions require the immediate use of epinephrine, oxygen, and intravenous steroids.

#### LIVER—

A moderate rise in serum glutamic oxaloacetic transaminase (SGOT) has been noted, particularly in infants, but the significance of this finding is unknown.

#### HEMIC AND LYMPHATIC SYSTEMS—

Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia, and agranulocytosis have been reported during therapy with the penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be sensitivity reactions.

#### Dosage

*Infections of the ear, nose, throat, and lower respiratory tract* due to streptococci, pneumococci, and non-penicillinase producing staphylococci; and also those infections of the upper and lower respiratory tract due to *H. influenzae*.

**Adults:** 250 mg. every 6 hours.

**Children:** 50 mg./kg./day in divided doses every 6 or 8 hours.

*Infections of the genitourinary tract caused by sensitive Gram negative and Gram positive bacteria.*

**Adults:** 500 mg. every 6 hours. Larger doses may be required for severe infections.

**Children:** 100 mg./kg./day in divided doses every 6 hours.

*Urethritis due to N. gonorrhoeae.*

**Adult Males:** 500 mg. every 8 hours.

*Cases of gonorrhea with a suspected lesion of syphilis should have dark-field examinations before receiving ampicillin, and monthly serological tests for a minimum of 4 months.*

*Infections of the gastrointestinal tract.*

**Adults:** 500 mg. every 6 hours.

**Children:** 100 mg./kg./day in divided doses every 6 hours.

Larger doses may be required for stubborn or severe infections. The children's dosage is intended for individuals whose weight will not cause a dosage to be calculated greater than that recommended for adults. Children weighing more than 20 kg. should be dosed according to the adult recommendations.

It should be recognized that in the treatment of chronic urinary tract and intestinal infections, frequent bacteriological and clinical appraisal are necessary. Smaller doses than those recommended above should not be used. Even higher doses may be needed at times. In stubborn infections, therapy may be required for several weeks. It may be necessary to continue clinical and/or bacteriological follow-up for several months after cessation of therapy.

Treatment should be continued for a minimum of 48 to 72 hours beyond the time that the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. It is recommended that there be at least 10 days' treatment for any infection caused by hemolytic streptococci, to help prevent the occurrence of acute rheumatic fever or glomerulonephritis.

#### Directions for Mixing Oral Suspension

Prepare suspension at time of dispensing as follows: Add 53 cc. of water to the 80 cc. package and 100 cc. of water to the 150 cc. package. Shake vigorously. This will provide 80 and 150 cc. of suspension, respectively. Each teaspoonful (5 cc.) will contain 125 mg. or 250 mg. TOTACILLIN (Ampicillin Trihydrate). The reconstituted suspension is stable for 7 days at room temperature and 14 days under refrigeration.

#### Supply

TOTACILLIN (Ampicillin Trihydrate) for Oral Suspension. Each 5 cc. of reconstituted suspension contains ampicillin trihydrate equivalent to 125 mg. or 250 mg. ampicillin.

125 mg./5 cc.

250 mg./5 cc.

List No. 9312..... 80 cc. bottle

List No. 9325..... 80 cc. bottle

List No. 9412.....150 cc. bottle

List No. 9425.....150 cc. bottle

BEECHAM PHARMACEUTICALS  
Division of Beecham Inc.  
Clifton, New Jersey 07012

Gummed Section

KEEP TIGHTLY CLOSED • SHAKE WELL BEFORE USING  
When stored at room temperature discard unused portion after 7 days;  
When stored under refrigeration discard unused portion after 14 days.

Control No.

Exp. Date

Tear along perforation

IMPORTANT: Read accompanying literature enclosed for indications, dosage and precautions.

**BEECHAM**

80 cc. (2 1/2 fl. oz.) No. 9312

**TOTACILLIN®**  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

equivalent to  
**2.0 Gm. Ampicillin**

WHEN RECONSTITUTED,  
EACH 5 cc. WILL CONTAIN

**125 mg.**

AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.

**BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

NDC 319-9312-03

Directions for Mixing

Add 53 cc. of water and shake vigorously. Each 5 cc. (1 teaspoonful)  
contains ampicillin trihydrate equivalent to 125 mg. ampicillin.

Usual dosage —  
Children: 50 - 100 mg./kg./day in divided doses every 6-8 hours.  
Adults: 250 - 500 mg. every 6 hours. 5271 MADE IN U.S.A.

Note Perforation

*Reviewed 4-27-70*  
*Abbey is acceptable*  
*has Dr. Zinner's MD*  
*Division of Int'l. Affairs Dept.*  
*effective*

"Tear off" Section

+

Exp. Date  
Control No.  
125 mg./5 cc.  
AMPICILLIN TRIHYDRATE  
**TOTACILLIN**<sup>®</sup>  
No. 9312

NDC 319-9312-03

**BEECHAM**

80 cc. (2 2/3 fl. oz.) No. 9312

**TOTACILLIN**<sup>®</sup>  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

equivalent to  
2.0 Gm. Ampicillin

WHEN RECONSTITUTED,  
EACH 5cc. WILL CONTAIN

**125 mg.**

AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.

**BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

Directions for Mixing :  
Prepare suspension at  
the time of dispensing.  
Add 53 cc. of water to  
the bottle and shake  
vigorously. This pro-  
vides 80 cc. of sus-  
pension. Each 5 cc. (1  
teaspoonful) contains  
ampicillin trihydrate  
equivalent to 125 mg.  
ampicillin.

When stored at room  
temperature discard  
unused portion after 7  
days; when stored  
under refrigeration  
discard unused por-  
tion after 14 days.

**KEEP BOTTLE  
TIGHTLY CLOSED**

5265  
2-70

4-27-70  
Date  
Graham is acceptable  
M. J. M. - Green Mt.  
BEECHAM  
DIVISION OF BEECHAM DRUGS  
injection



NDC 319-9312-03

**BEECHAM**

80 cc. (2 2/3 fl. oz.) No. 9312

Usual Dosage—

Children:  
50-100 mg./kg./day  
in divided doses  
every 6-8 hours.

Adults:  
250 - 500 mg. every 6  
hours.

**IMPORTANT:** Read  
the complete descrip-  
tive literature en-  
closed.

See top flap for  
Control Number and  
Expiration Date

MADE IN U.S.A.

**TOTACILLIN®**  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

equivalent to  
2.0 Gm. Ampicillin

WHEN RECONSTITUTED,  
EACH 5 cc. WILL CONTAIN

**125 mg.**

AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.



**BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

ROBERTSON  
MONTVILLE, CONN.

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*Handwritten notes:*  
- 27-70  
This  
Sachet is acceptable  
MAY 20 1970  
BEECHAM  
DIVISION OF ANTIBIOTIC DRUGS  
injection

Exp. Date

Control No.

**TOTACILLIN®**  
**AMPICILLIN TRIHYDRATE**  
125 mg./5 cc.

No. 9412

NDC 319-9312-06

**BEECHAM**

150 cc. (6 fl. oz.)

No. 9412

**TOTACILLIN®**  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

*equivalent to*  
*3.75 Gm. Ampicillin*

WHEN RECONSTITUTED,  
EACH 5 cc. WILL CONTAIN

**125 mg.**

AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.



**BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

Directions for Mixing:  
Prepare suspension at the time of dispensing. Add 100 cc. of water to the bottle and shake vigorously. This provides 150 cc. of suspension. Each 5 cc. (1 teaspoonful) contains ampicillin trihydrate equivalent to 125 mg. ampicillin.

When stored at room temperature discard unused portion after 7 days; when stored under refrigeration discard unused portion after 14 days.

**KEEP BOTTLE  
TIGHTLY CLOSED**

5266  
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Reviewed 4-27-70  
Date  
Labeling is acceptable  
Mar 28 70



NDC 319-9312-06

**BEECHAM**

150 cc. (6 fl. oz.) No. 9412

**Usual Dosage—**

Children:  
50-100 mg./kg./day  
in divided doses  
every 6-8 hours.

Adults:  
250 - 500 mg. every 6  
hours.

**IMPORTANT:** Read  
the complete descrip-  
tive literature en-  
closed.

See top flap for  
Control Number and  
Expiration Date

**TOTACILLIN<sup>®</sup>**  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

equivalent to  
3.75 Gm. Ampicillin

WHEN RECONSTITUTED,  
EACH 5 cc. WILL CONTAIN

**125 mg.**

AMPICILLIN

**CAUTION:** Federal law prohibits  
dispensing without prescription.

MADE IN U.S.A.



**BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012



2

Reviewed 4-27-70

Date Labeling is acceptable

*Mag. M. Jones, MD*  
MEDICAL OFFICER  
Division of Beecham Inc.

No. 9325  
**TOTACILLIN<sup>®</sup>**  
AMPICILLIN TRIHYDRATE  
250 mg./5 cc.  
Control No.  
Exp. Date

NDC 319-9325-03

**BEECHAM**

80 cc. (2 1/2 fl. oz.) No. 9325

**TOTACILLIN<sup>®</sup>**  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

equivalent to  
4.0 Gm. Ampicillin

WHEN RECONSTITUTED,  
EACH 5cc. WILL CONTAIN

**250 mg.**

AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.

**b** **BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

Directions for Mixing :  
Prepare suspension at  
the time of dispensing.  
Add 53 cc. of water to  
the bottle and shake  
vigorously. This pro-  
vides 80 cc. of sus-  
pension. Each 5 cc. (1  
teaspoonful) contains  
ampicillin trihydrate  
equivalent to 250 mg.  
ampicillin.

When stored at room  
temperature discard  
unused portion after 7  
days; when stored  
under refrigeration  
discard unused por-  
tion after 14 days.

**KEEP BOTTLE  
TIGHTLY CLOSED**

5519  
2-70



NDC 319-9325-03

**BEECHAM**

80 cc. (2 2/3 fl. oz.) No. 9325

Usual Dosage—

Children:  
50-100 mg./kg./day  
in divided doses  
every 6-8 hours.

Adults:  
250 - 500 mg. every 6  
hours.

**IMPORTANT:** Read  
the complete descrip-  
tive literature en-  
closed.

See top flap for  
Control Number and  
Expiration Date

MADE IN U.S.A.

**TOTACILLIN<sup>®</sup>**  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

*equivalent to*  
*4.0 Gm. Ampicillin*

WHEN RECONSTITUTED,  
EACH 5 cc. WILL CONTAIN

**250 mg.**

AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.



**BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012



1

Note Perforation

Gummed Section

KEEP TIGHTLY CLOSED • SHAKE WELL BEFORE USING  
When stored at room temperature discard unused portion after 7 days;  
when stored under refrigeration discard unused portion after 14 days.

Control No.

Exp. Date

Tear along perforation

IMPORTANT: Read accompanying literature enclosed for indications,  
dosage and precautions.

**BEECHAM**  
150 cc. (6 fl. oz.) No. 9425

**TOTACILLIN®**  
**AMPICILLIN TRIHYDRATE**  
for  
**ORAL SUSPENSION**  
equivalent to  
7.50 Gm. Ampicillin

WHEN RECONSTITUTED,  
EACH 5 cc. WILL CONTAIN

**250 mg.**  
AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.

**BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

NDC 319-9325-06

Directions for Mixing  
Add 100 cc. of water and shake vigorously. Each 5 cc. (1 teaspoonful)  
contains ampicillin trihydrate equivalent to 250 mg. ampicillin.

Usual dosage—  
Children: 50 - 100 mg. /kg. /day in divided doses every 6-8 hours.  
Adults: 250 - 500 mg. every 6 hours.

MADE IN U.S.A.  
5518

"Tear off" Section

Revised 4-27-70

Date

Labeling is acceptable

*Wm. J. ...*  
Medical Officer  
DIVISION OF ANTI-BIOTIC DRUGS  
*infectious*



Exp. Date  
Control No.  
250 mg./5 cc.  
**TOTACILLIN**  
AMPICILLIN TRIHYDRATE  
No. 9425

NDC 319-9325-06

**BEECHAM**

150 cc. (6 fl. oz.) No. 9425

**TOTACILLIN**<sup>®</sup>  
**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

equivalent to  
7.50 Gm. Ampicillin

WHEN RECONSTITUTED,  
EACH 5 cc. WILL CONTAIN

**250 mg.**

AMPICILLIN

CAUTION: Federal law prohibits  
dispensing without prescription.

**Directions for Mixing:**  
Prepare suspension at the time of dispensing. Add 100 cc. of water to the bottle and shake vigorously. This provides 150 cc. of suspension. Each 5 cc. (1 teaspoonful) contains ampicillin trihydrate equivalent to 250 mg. ampicillin.

When stored at room temperature discard unused portion after 7 days; when stored under refrigeration discard unused portion after 14 days.

**KEEP BOTTLE  
TIGHTLY CLOSED**

**b** **BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

5520  
2-70

Reviewed 4-27-70 Date  
Resubmitted to acceptable  
*Mrs. Ann L. Linn, M.D.*  
Medical Officer  
Division of Antibiotic Drugs

NDC 319-9325-06

**BEECHAM**

150 cc. (6 fl. oz.)

No. 9425

Usual Dosage—

Children:  
50-100 mg./kg./day  
in divided doses  
every 6-8 hours.

Adults:  
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hours.

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tive literature en-  
closed.

See top flap for  
Control Number and  
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**AMPICILLIN TRIHYDRATE**

for  
**ORAL SUSPENSION**

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7.50 Gm. Ampicillin

WHEN RECONSTITUTED,  
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**250 mg.**

AMPICILLIN

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MADE IN U.S.A.

**b** **BEECHAM PHARMACEUTICALS**  
DIV. OF BEECHAM INC., CLIFTON, N. J. 07012

ROBERTSON  
MONTVUE, VA

1

Reviewed 4-27-70

Date  
Labeling is acceptable

*Mary Ann Linn, MD*  
Medical Officer  
Division of Antibiotic Drugs  
*infective*

6 pages redacted from this section of  
the approval package consisted of draft labeling