AMOXICILLIN AND CLAVULANATE POTASSIUM - amoxicillin and clavulanate potassium powder, for suspension
Aurobindo Pharma Limited

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION safely and effectively. See full prescribing information for AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION.

AMOXICILLIN and CLAVULANATE POTASSIUM for oral suspension
Initial U.S. Approval: 1984

RECENT MAJOR CHANGES

Indications and Usage (1) 7/2026
Dosage and Administration (2) 7/2026

INDICATIONS AND USAGE

Amoxicillin and clavulanate potassium for oral suspension is a combination of amoxicillin, a penicillin-class antibacterial and clavulanate potassium, a beta-lactamase inhibitor, indicated for the treatment of infections caused by designated susceptible (confirmed or suspected) beta-lactamase-producing microorganisms (1):

Lower Respiratory Tract Infections (1.1)
- Amoxicillin and Clavulanate Potassium for Oral Suspension: pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

Acute Bacterial Sinusitis (1.3)
- Amoxicillin and Clavulanate Potassium for Oral Suspension: pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

Acute Bacterial Otitis Media (1.4)
- Amoxicillin and Clavulanate Potassium for Oral Suspension: pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

Skin and Skin Structure Infections (1.6)
- Amoxicillin and Clavulanate Potassium for Oral Suspension: pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

Urinary Tract Infections (1.7)

- Amoxicillin and Clavulanate Potassium for Oral Suspension: pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

Limitations of Use (1.8)

- Therapy may be initiated before bacteriological results are available when beta-lactamase-producing pathogens are suspected. When results show susceptibility to amoxicillin alone, amoxicillin and clavulanate potassium for oral suspension should not be used.

Usage to Reduce Development of Drug-Resistant Bacteria (1.9)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of amoxicillin and clavulanate potassium for oral suspension and other antibacterial drugs, amoxicillin and clavulanate potassium for oral suspension should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

DOSAGE AND ADMINISTRATION

- Recommended dosage and administration for the amoxicillin and clavulanate potassium depends on the indication, patient age, weight, and ability to swallow tablets. Therefore, carefully follow the recommended dosage and administration instructions specified below.

- Pediatric Patients 3 Months and Older and Weighing Less Than 40 kg (2.4)

Infection Type	Frequency	Dose	Formulation Strength
Amoxicillin and Clavulanate Potassium for Oral Suspension			
Mild to Moderate Infections	Every 12 hours	25 mg/kg/day divided into 2 doses	200 mg/28.5 mg or 400 mg/57 mg
	Every 8 hours	20 mg/kg/day divided into 3 doses	125 mg/31.25 mg or 250 mg/62.5 mg
Severe Infections	Every 12 hours	45 mg/kg/day divided into 2 doses	200 mg/28.5 mg or 400 mg/57 mg
	Every 8 hours	40 mg/kg/day divided into 3 doses	125 mg/31.25 mg or 250 mg/62.5 mg

- Adjust dose for severe renal impairment (GFR less than 30 mL/min) and in patients on hemodialysis. (2.6, 8.6, 12.3)
- See full Prescribing Information for preparation of oral suspension. (2.7, 2.8)

DOSAGE FORMS AND STRENGTHS

- Amoxicillin and Clavulanate Potassium for Oral Suspension: 200 mg/28.5 mg per 5 mL and 400 mg/57 mg per 5 mL (3)

CONTRAINDICATIONS

- History of a serious hypersensitivity reaction (e.g., anaphylaxis or Stevens-Johnson syndrome) to amoxicillin and clavulanate potassium for oral suspension or to other beta-lactams (e.g., penicillins and cephalosporins). (4.1)
- History of cholestatic jaundice/hepatic dysfunction associated with amoxicillin and clavulanate potassium for oral suspension. (4.2)

WARNINGS AND PRECAUTIONS

- Serious (including fatal) hypersensitivity reactions: Discontinue amoxicillin and clavulanate potassium for oral suspension if a reaction occurs and institute appropriate therapy. (5.1)
- Severe cutaneous adverse reactions (SCAR): Monitor closely. Discontinue if rash progresses. (5.2)
- Drug-induced enterocolitis syndrome (DIES): Discontinue if DIES occurs and institute appropriate therapy. (5.3)
- Hepatic dysfunction and cholestatic jaundice: Discontinue if signs/symptoms of hepatitis occur. Monitor liver function tests in patients with hepatic impairment. (5.4)
- *Clostridioides difficile*-associated diarrhea (CDAD): Evaluate patients if diarrhea occurs. (5.5)
- Patients with mononucleosis: Increased risk of skin rash. Avoid amoxicillin and clavulanate potassium use in these patients. (5.6)

ADVERSE REACTIONS

- The most frequently reported adverse reactions with amoxicillin and clavulanate potassium for oral suspension were (incidence ≥3%) diarrhea/loose stools, nausea, skin rash, and urticaria. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Aurobindo Pharma USA, Inc. at 1-866-850-2876 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

- Concomitant use with probenecid is not recommended. (7.1)
- Concomitant use with oral anticoagulants may increase the prolongation of prothrombin time. (7.2)
- Concomitant use with allopurinol increases the risk of rash. (7.3)

USE IN SPECIFIC POPULATIONS

Renal Impairment: Dosage adjustment is recommended for severe renal impairment (GFR <30 mL/min). (2.6, 8.6)

See 17 for PATIENT COUNSELING INFORMATION.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Lower Respiratory Tract Infections

Amoxicillin and clavulanate potassium for oral suspension is indicated for the treatment of lower respiratory tract infection due to confirmed or suspected beta-lactamase producing *Haemophilus influenzae* and *Moraxella catarrhalis* as follows *[see Clinical Pharmacology (12.4), Clinical Studies (14.1)]*:

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

1.3 Acute Bacterial Sinusitis

Amoxicillin and clavulanate potassium for oral suspension is indicated for the treatment of acute bacterial sinusitis due to confirmed or suspected beta-lactamase-producing *Haemophilus influenzae* and *Moraxella catarrhalis* as follows *[see Clinical Pharmacology (12.4), Clinical Studies (14.4)]:*

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in adult or pediatric patients who cannot swallow tablets

1.4 Acute Bacterial Otitis Media

Amoxicillin and clavulanate potassium for oral suspension is indicated for the treatment of acute bacterial otitis media due to confirmed or suspected beta-lactamase-producing *Haemophilus influenzae* and *Moraxella catarrhalis* as follows *[see Use in Specific Populations (8.4), Clinical Studies (14.5)]*:

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

1.6 Skin and Skin Structure Infections

Amoxicillin and clavulanate potassium for oral suspension is indicated for the treatment of skin and skin structure infections due to confirmed or suspected beta-lactamase-producing *S. aureus*, *Escherichia coli*, and *Klebsiella* species as follows *[see Use in Specific Populations (8.4)]*:

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

1.7 Urinary Tract Infections

Amoxicillin and clavulanate potassium for oral suspension is indicated for the treatment of urinary tract infections due to confirmed or suspected beta-lactamase-producing *E. coli*, *Klebsiella* species, and *Enterobacter* species as follows *[see Use in Specific Populations (8.4), Clinical Studies (14.2)]*:

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in adult and pediatric patients who cannot swallow tablets

1.8 Limitations of Use

- Therapy may be initiated before bacteriological results are available when beta-lactamase-producing pathogens are suspected. When results show susceptibility to amoxicillin alone, amoxicillin and clavulanate potassium for oral suspension should not be used.

1.9 Usage to Reduce Development of Drug-Resistant Bacteria

To reduce the development of drug-resistant bacteria and maintain the effectiveness of amoxicillin and clavulanate potassium for oral suspension and other antibacterial drugs, amoxicillin and clavulanate potassium for oral suspension should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

- The recommended dosage and administration for the amoxicillin and clavulanate potassium, depends on the indication, patient age, weight, and ability to swallow tablets. Therefore, carefully follow the recommended dosage and administration instructions specified below *[see Dosage and Administration (2.4, 2.6 to 2.8)]*.
- Substitution among amoxicillin and clavulanate potassium formulations should only occur when the amoxicillin-to-clavulanic acid ratio is matched; AUGMENTIN Chewable Tablets and Amoxicillin and Clavulanate Potassium for Oral Suspension are substitutable on a mg-per-mg basis, and certain AUGMENTIN Tablet strengths are substitutable with specific Amoxicillin and Clavulanate Potassium for Oral Suspension or AUGMENTIN Chewable Tablet strengths. *[see Dosage and Administration (2.8)]*.

2.4 Recommended Dosage of Amoxicillin and Clavulanate Potassium for Oral Suspension in Pediatric Patients Aged 3 Months and Older and Weighing Less Than 40 kg

The recommended dosage of amoxicillin and clavulanate potassium for oral suspension for pediatric patients aged 3 months and older and weighing less than 40 kg are provided in Table 2.

Amoxicillin and clavulanate potassium for oral suspension may be taken without regard to meals; however, absorption of clavulanate potassium is enhanced when amoxicillin and clavulanate potassium for oral suspension are administered at the start of a meal. To minimize the potential for gastrointestinal intolerance, amoxicillin and clavulanate potassium for oral suspension should be taken at the start of a meal.

Table 2: Recommended Dosage of Amoxicillin and Clavulanate Potassium for Oral Suspension in Pediatric Patients Aged 3 Months and Older and Weighing Less Than 40 kg

Infection Type	Frequency[a]	Dose (Amoxicillin component)	Formulation Strength
Amoxicillin and Clavulanate Potassium for Oral Suspension[b]			
Less Severe Infections	Every 12 hours	25 mg/kg/day divided into 2 doses	200 mg/28.5 mg or 400 mg/57 mg
	Every 8 hours	20 mg/kg/day divided into 3 doses	125 mg/31.25 mg or 250 mg/62.5 mg
Otitis media[c], sinusitis, lower respiratory tract infections, and more severe infections	Every 12 hours	45 mg/kg/day divided into 2 doses	200 mg/28.5 mg or 400 mg/57 mg
	Every 8 hours	40 mg/kg/day divided into 3 doses	125 mg/31.25 mg or 250 mg/62.5 mg

[a]The every 12 hours regimen is recommended as it is associated with less diarrhea *[see Adverse Reactions (6.1)].*

[b]Strength of amoxicillin/clavulanate potassium per 5 mL oral suspension

[c]The recommended duration of therapy for acute bacterial otitis media is 10 days

2.6 Recommended Dosage in Patients with Renal Impairment

Amoxicillin and Clavulanate Potassium for Oral Suspension

A reduced dosage is recommended in patients with severe renal impairment (see Table 4). No dosage adjustment is recommended in patients with mild to moderate renal impairment.

Table 4: Recommended Dosage of Amoxicillin and Clavulanate Potassium for Oral Suspension in Patients with Severe Renal Impairment

Patients with Severe Renal Impairment	**Dosage**
GFR 10 mL/min to less than 30 mL/min	500 mg or 250 mg every 12 hours, depending on the severity of the infection
GFR less than 10 mL/min	500 mg or 250 mg every 24 hours, depending on severity of the infection
Hemodialysis	500 mg or 250 mg every 24 hours, depending on severity of the infection Administer an additional dose both during and at the end of dialysis

Patients with a GFR of less than 30 mL/min should not receive the 875 mg/125 mg dose of amoxicillin and clavulanate potassium.

2.7 Preparation and Storage (after reconstitution) of Amoxicillin and Clavulanate Potassium for Oral Suspension

Prepare the oral suspension at time of dispensing as follows:

- Shake the bottle to loosen powder.
- Measure the total amount of water (see Table 5) to be added in two parts.
- Add 2/3 of the total required water, close the bottle, and shake vigorously.
- Add the remaining water, close, and shake again.
- Shake well before each use.
- Administer the reconstituted amoxicillin and clavulanate potassium for oral suspension, use a dosing spoon or medicine dropper to a pediatric patient.
- Rinse the dosing spoon or dropper after each use.

Storage

Store reconstituted amoxicillin and clavulanate potassium for oral suspension under refrigeration; discard after 10 days. A slight color change during storage is normal.

Table 5: Amount of Water for Mixing Amoxicillin and Clavulanate Potassium for Oral Suspension

Strength of Oral Suspension (amoxicillin/clavulanic acid)	Bottle Size	Amount of Water for Reconstitution
200 mg/28.5 mg per 5 mL	50 mL 75 mL 100 mL	52 mL 73 mL 98 mL
400 mg/57 mg per 5 mL	50 mL 75 mL 100 mL	49 mL 70 mL 94 mL

2.8 Switching Between Dosage Forms and Strengths

Amoxicillin and Clavulanate Potassium for Oral Suspension

- Substitution among amoxicillin and clavulanate potassium formulations should only occur when the amoxicillin-to-clavulanic acid ratio is matched; AUGMENTIN Chewable Tablets and Amoxicillin and Clavulanate Potassium for Oral Suspension are substitutable on a mg-per-mg basis, and certain AUGMENTIN Tablet strengths are substitutable with specific Amoxicillin and Clavulanate Potassium for Oral Suspension or AUGMENTIN Chewable Tablet strengths.
- AUGMENTIN Chewable Tablets and Amoxicillin and Clavulanate Potassium for Oral Suspension formulations are for pediatric patients weighing less than 40 kg and in pediatric patients who cannot swallow tablets and may be substituted for each other where appropriate.

Table 6 provides guidance on selecting the appropriate strength when switching between AUGMENTIN Tablets and Amoxicillin and Clavulanate Potassium for Oral Suspension or AUGMENTIN Chewable Tablets to ensure the appropriate amoxicillin-to-clavulanic acid ratio.

Table 6: Selecting Appropriate Strengths of Amoxicillin and Clavulanate Potassium When Switching Between Tablets, Oral Suspension, or Chewable Tablets

AUGMENTIN Tablet Strength	Substitutable Strength of Amoxicillin and Clavulanate Potassium for Oral Suspension or AUGMENTIN Chewable Tablets[a]
250 mg/125 mg[b]	No equivalent available
500 mg/125 mg[c]	125 mg/31.25 mg or 250 mg/62.5 mg
875 mg/125 mg	200 mg/28.5 mg or 400 mg/57 mg
1,000 mg/62.5 mg	Not substitutable with immediate-release formulations

[a]One Chewable Tablet has the same amount of amoxicillin and clavulanic acid as 5 mL of the corresponding strength of Oral Suspension. Chewable tablets may only be used as a substitute in pediatric patients weighing less than 40 kg.

[b]AUGMENTIN 250 mg/125 mg tablet is NOT substitutable with AUGMENTIN 250 mg/62.5 mg chewable tablet.

[c]Two AUGMENTIN 250 mg/125 mg Tablets are not substitutable with one AUGMENTIN 500 mg/125 mg Tablet.

3 DOSAGE FORMS AND STRENGTHS

- **200 mg/28.5 mg per 5 mL:**White to off-white granular powder – Each 5 mL of reconstituted white to pale yellow, orange flavored suspension contains 200 mg of amoxicillin (as amoxicillin trihydrate) and 28.5 mg of clavulanic acid as the potassium salt.
- **400 mg/57 mg per 5 mL:** White to off-white granular powder – Each 5 mL of reconstituted white to pale yellow, orange flavored suspension contains 400 mg of amoxicillin (as amoxicillin trihydrate) and 57 mg of clavulanic acid as the potassium salt.

4 CONTRAINDICATIONS

4.1 Serious Hypersensitivity Reactions

Amoxicillin and clavulanate potassium for oral suspension is contraindicated in patients with a history of serious hypersensitivity reactions (e.g., anaphylaxis or Stevens-Johnson syndrome) to amoxicillin, clavulanate or to other beta-lactam antibacterial drugs (e.g., penicillins and cephalosporins).

4.2 Cholestatic Jaundice/Hepatic Dysfunction

Amoxicillin and clavulanate potassium for oral suspension is contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with treatment with amoxicillin/clavulanate potassium.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Allergic Reactions, including Anaphylaxis

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam antibacterials. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. Before initiating therapy with amoxicillin and clavulanate potassium, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. Amoxicillin and clavulanate potassium is contraindicated in patients with a history of serious hypersensitivity reactions to amoxicillin, clavulanate, or to other beta-lactam antibacterial drugs *[see Contraindications (4.1)].* If an allergic reaction occurs, discontinue amoxicillin and clavulanate potassium and institute appropriate therapy.

5.2 Severe Cutaneous Adverse Reactions (SCAR)

Amoxicillin and clavulanate potassium may cause severe cutaneous adverse reactions (SCAR), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP). If patients develop a skin rash, they should be monitored closely, and amoxicillin and clavulanate potassium discontinued if lesions progress.

5.3 Drug-Induced Enterocolitis Syndrome (DIES)

Drug-induced enterocolitis syndrome (DIES) has been reported with use of amoxicillin, a component of amoxicillin and clavulanate potassium for oral suspension *[see Adverse Reactions (6.2)]*, with most cases occurring in pediatric patients. DIES is a non-IgE mediated hypersensitivity reaction characterized by protracted vomiting occurring 1 to 4 hours after drug ingestion in the absence of skin or respiratory symptoms. DIES may be associated with pallor, lethargy, hypotension, shock, diarrhea within 24 hours after ingesting amoxicillin, and leukocytosis with neutrophilia. If DIES occurs, discontinue amoxicillin and clavulanate potassium and institute appropriate therapy.

5.4 Hepatic Dysfunction

Hepatic dysfunction, including hepatitis and cholestatic jaundice has been associated with the use of amoxicillin and clavulanate potassium. Hepatotoxicity is usually reversible; however, deaths have been reported. These cases have generally been associated with serious underlying diseases or concomitant medications. Amoxicillin and clavulanate potassium is contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with treatment with amoxicillin and clavulanate potassium *[see Contraindications (4.2), Use in Specific Populations (8.7), Adverse Reactions (6.2)]*.

5.5 *Clostridioides difficile*-Associated Diarrhea (CDAD)

Clostridioides difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including amoxicillin and clavulanate potassium, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin-producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

5.6 Skin Rash in Patients with Mononucleosis

A high percentage of patients with mononucleosis who receive amoxicillin develop an erythematous skin rash. Avoid amoxicillin and clavulanate potassium use in patients with mononucleosis *[see Adverse Reactions (6.2)].*

5.7 Potential for Microbial Overgrowth

The possibility of superinfections with mycotic or bacterial pathogens should be considered during therapy. If superinfections occur (commonly involving *Pseudomonas* spp. or *Candida* spp.), discontinue amoxicillin and clavulanate potassium and institute appropriate therapy.

5.8 Risks in Patients with Phenylketonuria

Phenylalanine can be harmful to patients with phenylketonuria (PKU). Amoxicillin and clavulanate potassium for oral suspension contain aspartame, which is a source of phenylalanine. Each 5 mL of the 200 mg/28.5 mg per 5 mL oral suspension contains 4.42 mg phenylalanine and each 5 mL of the 400 mg/57 mg per 5 mL oral suspension contains 6.35 mg phenylalanine. Before prescribing the amoxicillin and clavulanate potassium for oral suspension to patients with PKU, consider the combined daily amount of phenylalanine from all sources, including amoxicillin and clavulanate potassium.

5.9 Development of Drug-Resistant Bacteria

Prescribing amoxicillin and clavulanate potassium in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Serious Allergic Reactions, including Anaphylaxis *[see Warnings and Precautions (5.1)]*
- Severe Cutaneous Adverse Reactions *[see Warnings and Precautions (5.2)]*
- Drug-Induced Enterocolitis Syndrome (DIES) *[see Warnings and Precautions (5.3)]*
- Hepatic Dysfunction *[see Warnings and Precautions (5.4)]*
- *Clostridioides difficile*-associated diarrhea (CDAD) *[see Warnings and Precautions (5.5)]*
- Skin Rash in Patients with Mononucleosis *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Amoxicillin and Clavulanate Potassium for Oral Suspension

The most frequently reported adverse reactions in clinical trials were diarrhea/loose

stools (9%), nausea (3%), skin rash and urticaria (3%), vomiting (1%) and vaginitis (1%). Less than 3% of patients discontinued therapy due to adverse reactions. The overall incidence of adverse reactions, particularly diarrhea, increased with higher recommended doses. Other less frequently reported adverse reactions (˂1%) included abdominal discomfort, flatulence, and headache.

In two pivotal trials in adults with lower respiratory tract or urinary tract infections, the overall incidence of adverse reactions was similar between AUGMENTIN 875 mg/125 mg Tablets every 12 hours and AUGMENTIN 500 mg/125 mg Tablets every 8 hours *[see Clinical Studies (14.1, 14.2)]*. The most common adverse reaction was diarrhea, reported in 15% of patients receiving AUGMENTIN 875 mg/125 mg every 12 hours and 14% of patients receiving AUGMENTIN 500 mg/125 mg every 8 hours. The rate of severe diarrhea or discontinuation due to diarrhea was 1% versus 2%, respectively.

In a controlled clinical trial of pediatric patients aged 2 months to 12 years with acute otitis media *[see Clinical Studies (14.5)]*, diarrhea was defined in the protocol as ≥3 watery stools or ≥4 loose/watery stools in 1 day, or ≥2 watery stools or ≥3 loose/watery stools per day for 2 consecutive days, as recorded on diary cards. The incidence of diarrhea was significantly lower in patients treated with amoxicillin and clavulanate potassium for oral suspension 45 mg/kg/day divided every 12 hours (14%) compared to patients treated with amoxicillin and clavulanate potassium for oral suspension 40 mg/kg/day divided every 8 hours (34%). It is not known whether the statistically significant reduction in diarrhea with the oral suspension dosed every 12 hours, versus suspensions dosed every 8 hours, can be extrapolated to the chewable tablets, all of which contain mannitol. The presence of mannitol in the chewable tablets may contribute to a different diarrhea profile. Severe diarrhea or discontinuation due to diarrhea occurred in 3% and 8% of patients, respectively. Allergic reactions leading to discontinuation occurred in 1% and <1% of patients, and candidal infection of the diaper area was reported in 4% and 6% of patients, respectively.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of amoxicillin and clavulanate potassium product. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal: Drug-induced enterocolitis syndrome (DIES), diarrhea, nausea, vomiting,indigestion, gastritis, stomatitis, glossitis, black “hairy” tongue, mucocutaneous candidiasis, enterocolitis, and hemorrhagic/pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment *[see Warnings and Precautions (5.3, 5.5)]*.

Immune: Hypersensitivity reactions, anaphylactic reactions (including shock), angioedema, serum sickness-like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, myalgia, and frequently fever), hypersensitivity vasculitis *[see Warnings and Precautions (5.1)].*

Skin and Appendages: Rashes, pruritus, urticaria, erythema multiforme, SJS, TEN, DRESS, AGEP, exfoliative dermatitis, and linear IgA bullous dermatosis *[see Warnings and Precautions (5.1, 5.2, 5.6)].*

Liver: A moderate rise in AST (SGOT) and/or ALT (SGPT) has been noted in patients treated with ampicillin-class antibacterials. Hepatic dysfunction, including increases in serum transaminases (AST and/or ALT), serum bilirubin, and/or alkaline phosphatase, has been reported with amoxicillin and clavulanate potassium. It has been reported more commonly in the elderly, in males, or in patients on prolonged treatment. The histologic findings on liver biopsy have consisted of cholestatic, hepatocellular, or mixed cholestatic-hepatocellular changes. The onset of signs/symptoms of hepatic dysfunction may occur during or several weeks after therapy has been discontinued. The hepatic dysfunction, which may be severe, is usually reversible. Deaths have been reported *[see Contraindications (4.2), Warnings and Precautions (5.4)]*.

Renal: Interstitial nephritis and hematuria have been reported. Crystalluria has also been reported *[see Overdosage (10)]*.

Hemic and Lymphatic Systems: Anemia, including hemolytic anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, and agranulocytosis have been reported during therapy with penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. There have been reports of increased prothrombin time in patients receiving amoxicillin and clavulanate potassium and anticoagulant therapy concomitantly *[see Drug Interactions (7.2)].*

Central Nervous System: Agitation, anxiety, behavioral changes, aseptic meningitis, confusion, convulsions, dizziness, insomnia, and reversible hyperactivity have been reported.

Miscellaneous: Tooth discoloration (brown, yellow, or gray staining) has been reported. Most reports occurred in pediatric patients. Discoloration was reduced or eliminated with brushing or dental cleaning in most cases.

7 DRUG INTERACTIONS

7.1 Probenecid

Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with amoxicillin and clavulanate potassium may result in increased and prolonged blood levels of amoxicillin. Co-administration of probenecid is not recommended.

7.2 Oral Anticoagulants

Abnormal prolongation of prothrombin time (increased international normalized ratio [INR]) has been reported in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

7.3 Allopurinol

The concurrent administration of allopurinol and amoxicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving amoxicillin alone. It is not known whether this potentiation of amoxicillin rashes is due to allopurinol or the hyperuricemia present in these patients. Discontinue allopurinol at the first appearance of skin rash when used concomitantly with amoxicillin and clavulanate potassium.

7.4 Interference of Amoxicillin and Clavulanate Potassium with Glucose Test

High urine concentrations of amoxicillin may result in false-positive reactions when testing for the presence of glucose in urine using CLINITEST®, Benedict's Solution, or Fehling's Solution. Therefore, it is recommended that glucose tests based on enzymatic glucose oxidase reactions be used.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from published epidemiologic studies and pharmacovigilance case reports over several decades of use with amoxicillin and clavulanate during pregnancy have not established a drug-associated risk of major birth defects, miscarriage, or adverse maternal outcomes. A study in women with preterm prelabor rupture of membranes (PPROM) reported that prophylactic treatment with amoxicillin and clavulanate may be associated with an increased risk of necrotizing enterocolitis in neonates *(see Data)*. Reproduction studies conducted in pregnant rats, given doses greater than or equal to 4 and 10 times the Maximum Recommended Human Dose (MRHD) of amoxicillin trihydrate and clavulanate respectively in amoxicillin and clavulanate potassium based on body surface area, revealed no evidence of fetal harm *(see Data)*.

The background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Human Data

One randomized, controlled trial included 4,826 pregnant women with premature rupture of fetal membranes who were randomly assigned to 250 mg erythromycin (n=1,197), 250 mg amoxicillin and 125 mg clavulanate (n=1,212), amoxicillin and clavulanate plus erythromycin (n=1,192), or placebo (n=1,225) four times daily for 10 days or until delivery. Amoxicillin and clavulanate was associated with a significantly increased rate of proven neonatal necrotizing enterocolitis: 1.9% (n=24) in the amoxicillin and clavulanate only group versus 0.5% (n=6) in the placebo group (p=0.001), and 1.8% (n=44) in the any amoxicillin and clavulanate group versus 0.7% (n=17) in the no amoxicillin and clavulanate group (p=0.0005).

Animal Data

In an embryofetal developmental study in pregnant rats, amoxicillin and clavulanate (2:1 ratio formulation of amoxicillin:clavulanate) were administered at oral doses up to 1,200 mg/kg/day during the period of organogenesis (gestation days (GD) 6 to 15). No evidence of fetal harm was observed. Based on body surface area comparisons, the dose corresponds to approximately 4 times the MRHD for amoxicillin trihydrate and 10 times the MRHD for clavulanate potassium.

In a pre-and postnatal developmental study in pregnant rats, amoxicillin and clavulanate (2:1 ratio formulation of amoxicillin:clavulanate) were administered at oral doses up to 1,200 mg/kg/day beginning from GD 15 through Day 21 of lactation. No effects on maternal reproductive function or on developmental and reproductive parameters of the offspring were observed up to the highest dose, corresponding to approximately 4 times the MRHD for amoxicillin trihydrate and 10 times the MRHD for clavulanate potassium, based on body surface area comparisons.

8.2 Lactation

Risk Summary

Data from a published clinical lactation study report that amoxicillin is present in human milk. There are reports of diarrhea, irritability, and rash in infants exposed to amoxicillin and clavulanate through breast milk; therefore, infants exposed to amoxicillin and clavulanate potassium should be monitored for these symptoms. There are no data on the effects of amoxicillin and clavulanate on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for amoxicillin and clavulanate potassium and any potential adverse effects on the breastfed child from amoxicillin and clavulanate potassium or from the underlying maternal condition.

8.4 Pediatric Use

The five amoxicillin and clavulanate potassium dosage forms (tablets, chewable tablets, oral suspension, XR tablets, and ES-600 for oral suspension) are different products. They are approved for different pediatric indications, age groups, and weights; have different dosing regimens; and have different preparation and administration

instructions. Therefore, select the recommended dosage form based on the pediatric indication, age group, and weight *[see Dosage and Administration (2)].*

Lower Respiratory Tract Infections

The safety and effectiveness of amoxicillin and clavulanate potassium have been established for the treatment of lower respiratory tract infections due to confirmed or suspected beta-lactamase producing isolates of *Haemophilus influenzae* and *Moraxella catarrhalis* as follows *[see Indications and Usage (1.1), Clinical Pharmacology (12.3), Clinical Studies (14.1)]*:

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in pediatric patients who cannot swallow tablets. Effectiveness is supported by adequate and well-controlled studies in adults, with pediatric pharmacokinetic data bridging to the less than 40 kg population.

Acute Bacterial Sinusitis

The safety and effectiveness of amoxicillin and clavulanate potassium for oral suspension have been established for the treatment of acute bacterial sinusitis due to confirmed or suspected beta-lactamase-producing *Haemophilus influenzae* and *Moraxella catarrhalis* as follows *[see Indications and Usage (1.3), Clinical Pharmacology (12.3), Clinical Studies (14.4)]*:

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in pediatric patients who cannot swallow tablets. Effectiveness is supported by adequate and well-controlled studies in adults, with pediatric pharmacokinetic data bridging to the less than 40 kg pediatric population.

Acute Bacterial Otitis Media

The safety and effectiveness of amoxicillin and clavulanate potassium have been established for the treatment of acute bacterial otitis media due to confirmed or suspected beta-lactamase-producing *Haemophilus influenzae* and *Moraxella catarrhalis* as follows *[see Indications and Usage (1.4), Clinical Pharmacology (12.3), Clinical Studies (14.5)]*:

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in pediatric patients who cannot swallow tablets. Effectiveness is supported by adequate and well-controlled studies conducted in adults, with additional data from a study conducted in pediatric patients with acute bacterial otitis media aged 2 months to 12 years.

Skin and Skin Structure Infections

The safety and effectiveness of amoxicillin and clavulanate potassium have been established for the treatment of skin and skin structure infections due to confirmed or suspected beta-lactamase-producing *S. aureus*, *Escherichia coli*, and *Klebsiella* species as follows *[see Indications and Usage (1.6), Clinical Pharmacology (12.3)]:*

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in pediatric patients who cannot swallow tablets. Effectiveness is supported by adequate and well-controlled studies conducted in pediatric patients.

Urinary Tract Infections

The safety and effectiveness of amoxicillin and clavulanate potassium have been established for the treatment of urinary tract infections due to confirmed or suspected beta-lactamase-producing *E. coli*, *Klebsiella* species, and *Enterobacter* species as follows *[see Indications and Usage (1.7), Clinical Pharmacology (12.3), Clinical Studies (14.2)]:*

- **Amoxicillin and Clavulanate Potassium for Oral Suspension:** pediatric patients weighing less than 40 kg, and in pediatric patients who cannot swallow tablets. Effectiveness is supported by adequate and well-controlled studies conducted in pediatric patients.

Use Not Established in Certain Pediatric Populations

The safety and effectiveness of amoxicillin and clavulanate potassium have not been established in the following pediatric populations:

- AUGMENTIN ES-600 for Oral Suspension in pediatric patients less than 3 months of age, or pediatric patients 3 months to 12 years of age weighing more than 40 kg
- AUGMENTIN Tablets and AUGMENTIN XR Extended-Release Tablets in pediatric patients weighing less than 40 kg, due to different amoxicillin-to-clavulanate ratios from the Chewable Tablets and for Oral Suspension formulations *[see Dosage and Administration (2.4)].*

Data are insufficient to support extrapolation in these age groups due to developmental differences in renal function. Elimination of amoxicillin may be delayed, while clavulanate elimination is not altered. Dosage should be modified in pediatric patients less than 12 weeks (3 months) *[see Dosage and Administration (2.3)].*

8.5 Geriatric Use

Amoxicillin and clavulanate potassium is substantially excreted by the kidney, and the risk of adverse reactions to amoxicillin and clavulanate potassium may be greater in patients with renal impairment than in patients with normal renal function. Because geriatric patients are more likely to have renal impairment, monitor for adverse reactions. Dosage adjustment is recommended in patients with severe renal impairment *[see Dosage and Administration (2.6)*, *Use in Specific Populations (8.6)]*.

8.6 Renal Impairment

Amoxicillin is primarily eliminated by the kidney. Both amoxicillin and clavulanate are removed from the circulation by hemodialysis.

Amoxicillin and Clavulanate Potassium

No dosage adjustment is recommended in patients with mild to moderate renal impairment. A reduced dosage is recommended in patients with severe renal impairment (GFR less than 30 mL/min). Patients with a GFR of less than 30 mL/min should not receive the 875 mg/125 mg dose of amoxicillin and clavulanate potassium *[see Dosage and Administration (2.6)]*.

8.7 Hepatic Impairment

Monitor hepatic function as appropriate during therapy with amoxicillin and clavulanate potassium *[see Contraindications (4.2), Warnings and Precautions (5.4)]*.

10 OVERDOSAGE

Following overdosage, patients have experienced primarily gastrointestinal symptoms including stomach and abdominal pain, vomiting, and diarrhea. Rash, hyperactivity, or drowsiness have also been observed in a small number of patients.

In the case of overdosage, discontinue amoxicillin and clavulanate potassium, treat symptomatically, and institute supportive measures as required. A prospective study of 51 pediatric patients at a poison control center suggested that overdosages of less than 250 mg/kg of amoxicillin are not associated with significant clinical symptoms and do not require gastric emptying.[1] Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

Interstitial nephritis resulting in oliguric renal failure has been reported in a small number of patients after overdosage with amoxicillin.

Crystalluria, in some cases leading to renal failure, has also been reported after amoxicillin overdosage in adult and pediatric patients. In case of overdosage, adequate fluid intake and diuresis should be maintained to reduce the risk of amoxicillin crystalluria.

Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of both amoxicillin and clavulanate. Both amoxicillin and clavulanate are removed from the circulation by hemodialysis.

11 DESCRIPTION

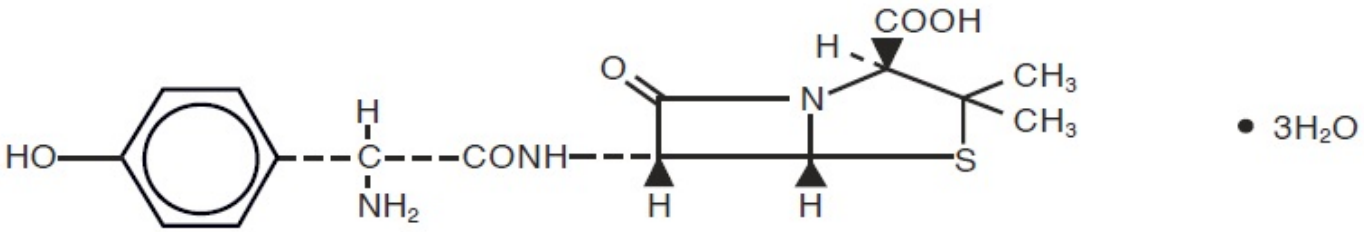
Amoxicillin and clavulanate potassium for oral suspension, USP is an oral antibacterial combination consisting of the semisynthetic antibacterial amoxicillin and the beta-lactamase inhibitor clavulanate potassium (the potassium salt of clavulanic acid).

- In amoxicillin and clavulanate potassium for oral suspension, USP, amoxicillin is present as amoxicillin trihydrate.

Amoxicillin USP is an analog of ampicillin, derived from the basic penicillin nucleus, 6-aminopenicillanic acid.

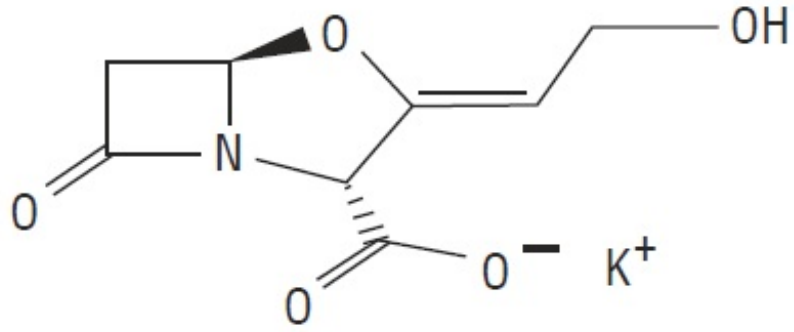
Amoxicillin trihydrate has a molecular formula of $C_{16}H_{19}N_3O_5S \cdot 3H_2O$, and a molecular weight of 419.46. Chemically, it is (2*S*,5*R*,6*R*)-6-[(*R*)-(-)-2-Amino-2-(*p*-hydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-

carboxylic acid trihydrate and may be represented structurally as:



Clavulanic acid is produced by the fermentation of *Streptomyces clavuligerus*. It is a beta-lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of beta-lactamases by blocking the active sites of these enzymes. Clavulanic acid is particularly active against the clinically important plasmid-mediated beta-lactamases frequently responsible for transferred drug resistance to penicillins and cephalosporins.

Clavulanate potassium has a molecular formula of $C_8H_8KNO_5$ and a molecular weight of 237.25. Chemically, clavulanate potassium is potassium (*Z*)(2*R*,5*R*)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]-heptane-2-carboxylate and may be represented structurally as:



- **200 mg/28.5 mg:** Following constitution, each 5 mL of oral suspension contains 200 mg of amoxicillin (equivalent to 230 mg of amoxicillin trihydrate) and 28.5 mg of clavulanic acid (equivalent to 34 mg of clavulanate potassium).
- **400 mg/57 mg:** Following constitution, each 5 mL of oral suspension contains 400 mg of amoxicillin (equivalent to 460 mg of amoxicillin trihydrate) and 57 mg of clavulanic acid (equivalent to 68 mg of clavulanate potassium).

Amoxicillin and clavulanate potassium for oral suspension, USP is white to off-white granular powder and becomes white to pale yellow with orange flavored suspension after reconstitution.

- Each 5 mL of reconstituted 200 mg/28.5 mg oral suspension of amoxicillin and clavulanate contains 6 mg potassium.

- Each 5 mL of reconstituted 400 mg/57 mg oral suspension of amoxicillin and clavulanate contains 12 mg potassium.

Inactive Ingredients:

Colloidal silicon dioxide, hypromellose, orange flavour, silicon dioxide, succinic acid, xanthan gum and aspartame *[see Warnings and Precautions (5.8)].*

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Amoxicillin and clavulanate potassium is an antibacterial drug *[see Clinical Pharmacology (12.4)].*

12.2 Pharmacodynamics

The antibacterial activity of amoxicillin/clavulanate is primarily driven by the percentage of the dosing interval during which unbound (free) amoxicillin plasma concentrations exceed the minimum inhibitory concentration (%*f*T>MIC) of the target bacterial organism. Clavulanate inhibits β-lactamase enzymes and thereby restores activity of amoxicillin against certain β-lactamase–producing bacteria.

12.3 Pharmacokinetics

Absorption

Amoxicillin and Clavulanate Potassium for Oral Suspension

Dosing in the fasted or fed state has minimal effect on the pharmacokinetics of amoxicillin. While amoxicillin and clavulanate potassium can be given without regard to meals, absorption of clavulanate potassium when taken with food is greater relative to the fasted state. In one study, the relative bioavailability of clavulanate was reduced when amoxicillin and clavulanate potassium was dosed at 30 and 150 minutes after the start of a high-fat breakfast.

Amoxicillin and Clavulanate Potassium for Oral Suspension and Chewable Tablets

Mean pharmacokinetic parameters in healthy adult subjects following administration of amoxicillin and clavulanate potassium for oral suspension and chewable tablets are shown in Table 8.

Table 8: Mean (±S.D.) Amoxicillin and Clavulanate Potassium Pharmacokinetic Parameters[a,b] with Amoxicillin and Clavulanate Potassium for Oral Suspension and Chewable Tablets

Dose of Amoxicillin and Clavulanate Potassium	**C_{max} (mcg/mL)**		**AUC_{0-24} (mcg*h/mL)**	
Amoxicillin and Clavulanate potassium	Amoxicillin	Clavulanate potassium	Amoxicillin	Clavulanate potassium
400 mg/57 mg (5 mL of suspension)	6.94 ± 1.24	1.1 ± 0.42	17.29 ± 2.28	2.34 ± 0.94
400 mg/57 mg (1 chewable tablet)	6.67 ± 1.37	1.03 ± 0.33	17.24 ± 2.64	2.17 ± 0.73

[a]Mean (± standard deviation) values of 28 healthy adult subjects. Peak concentrations occurred

~1 hour post-dose.

[b]Administered at the start of a light meal.

Distribution

The protein binding of amoxicillin and clavulanic acid to human serum is approximately 18% and 25%, respectively. Amoxicillin diffuses readily into most body tissues and fluids, with the exception of the brain and spinal fluid.

Metabolism and Excretion

The half-life of amoxicillin after the oral administration of amoxicillin and clavulanate potassium is approximately 1.3 hours and that of clavulanic acid is approximately 1 hour.

Amoxicillin and Clavulanate Potassium for Oral Suspension

Following administration of a single 250 mg/125 mg or 500 mg/125 mg tablet, approximately 50 to 70% of amoxicillin and approximately 25 to 40% of clavulanic acid are excreted unchanged in urine during the first 6 hours.

Specific Populations:

Pediatric Patients:

Amoxicillin and Clavulanate Potassium for Oral Suspension

Two hours after administration of a single 35 mg/kg oral dose of amoxicillin and clavulanate potassium for oral suspension to fasting pediatrics, mean concentrations of 3 mcg/mL of amoxicillin and 0.5 mcg/mL of clavulanic acid were detected in middle ear effusions.

Drug Interaction Studies

Clinical Studies

Concurrent administration of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanic acid *[see Drug Interactions (7.1)]*.

12.4 Microbiology

Mechanism of Action

Amoxicillin binds to penicillin-binding proteins within the bacterial cell wall and inhibits bacterial cell wall synthesis. Clavulanic acid is a beta-lactam, structurally related to penicillin, that may inactivate certain beta-lactamase enzymes.

Resistance

Resistance to penicillins may be mediated by destruction of the beta-lactam ring by a beta-lactamase, altered affinity of penicillin for target, or decreased penetration of the antibacterial drug to reach the target site. Amoxicillin alone is susceptible to degradation by beta-lactamases, and therefore its spectrum of activity does not include bacteria that produce these enzymes.

Antimicrobial Activity

Amoxicillin and clavulanic acid has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections *[see Indications and Usage (1)].*

Lower Respiratory Tract Infections

Gram-negative bacteria:

Haemophilus influenzae

Moraxella catarrhalis

Acute Bacterial Sinusitis

Gram-positive bacteria:

Staphylococcus aureus (methicillin-susceptible)

Streptococcus pneumoniae

Gram-negative bacteria:

Haemophilus influenzae

Haemophilus parainfluenzae

Klebsiella pneumoniae

Moraxella catarrhalis

Acute Bacterial Otitis Media

Gram-positive bacteria:

Streptococcus pneumoniae

Gram-negative bacteria:

Haemophilus influenzae

Moraxella catarrhalis

Skin and Skin Structure Infections

Gram-positive bacteria:

Staphylococcus aureus (methicillin-susceptible)

Gram-negative bacteria:

Escherichia coli

Klebsiella spp.

Urinary Tract Infections

Gram-negative bacteria (including beta-lactamase-producing strains):

Escherichia coli

Klebsiella spp.

Enterobacter spp.

The following *in vitro* data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for amoxicillin and clavulanic acid against isolates of similar genus or organism group. However, the efficacy of amoxicillin and clavulanic acid in treating clinical infections caused by these bacteria have not been established in adequate and well-controlled trials.

Gram-positive bacteria:

Enterococcus faecalis

Staphylococcus epidermidis

Staphylococcus saprophyticus

Streptococcus pyogenes

Viridans group Streptococcus

Gram-negative Bacteria

Eikenella corrodens

Proteus mirabilis

Anaerobic Bacteria

Bacteroides species including Bacteroides fragilis

Fusobacterium species

Peptostreptococcus species

Susceptibility Testing:

For specific information regarding susceptibility test interpretive criteria and associated test methods and quality control standards recognized by FDA for this drug, please see https://www.fda.gov/STIC.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies in animals have not been performed to evaluate carcinogenic potential.

Mutagenesis

Amoxicillin and clavulanate (4:1 ratio formulation of amoxicillin:clavulanate) was non-mutagenic in the Ames bacterial mutation assay, and the yeast gene conversion assay. Amoxicillin and clavulanate was weakly positive in the mouse lymphoma assay, but the trend toward increased mutation frequencies in this assay occurred at concentrations that were also associated with decreased cell survival. Amoxicillin and clavulanate was negative in the mouse micronucleus test, and in the dominant lethal assay in mice. Clavulanate potassium alone was tested in the Ames bacterial mutation assay and in the mouse micronucleus test and was negative in each of these assays.

Impairment of Fertility

Amoxicillin and clavulanate (2:1 ratio formulation of amoxicillin:clavulanate) at oral doses of up to 1,200 mg/kg/day was found to have no effect on fertility and reproductive performance in rats. Based on body surface area comparisons, these doses correspond to approximately 4 times the MRHD for adults for amoxicillin trihydrate and 10 times the MRHD for clavulanate potassium.

14 CLINICAL STUDIES

14.1 Lower Respiratory Tract Infections in Adults Treated with AUGMENTIN Tablets

A randomized, controlled trial was conducted in 562 adults with lower respiratory tract infections, comparing AUGMENTIN 875 mg/125 mg every 12 hours with AUGMENTIN 500 mg/125 mg every 8 hours. Comparable efficacy was demonstrated between the two regimens.

14.2 Complicated Urinary Tract Infections in Adults Treated with AUGMENTIN Tablets

A randomized, controlled trial was conducted in adults with pyelonephritis (n=361) or complicated urinary tract infection (n=268), defined as urinary tract abnormalities that predispose to relapse after bacteriuria eradication. Patients were randomized 1:1 to receive AUGMENTIN 875 mg/125 mg every 12 hours (n=308) or AUGMENTIN 500 mg/125 mg every 8 hours (n=321). Among bacteriologically evaluable patients, bacteriologic success rates were comparable between the two dosing regimens when assessed immediately after therapy and at follow-up visits.

Table 13: Bacteriologic Efficacy Rates in Complicated Urinary Tract Infections in Adults

Time Post Therapy	875 mg every 12 hours % (n)	500 mg every 8 hours % (n)
2 to 4 days	81% (58)	80% (54)
5 to 9 days	58% (41)	52% (52)
2 to 4 weeks	52% (101)	55% (104)

14.4 Acute Bacterial Sinusitis in Adult and Pediatric Patients Weighing ≥40 kg Treated with AUGMENTIN XR Extended-Release Tablets

Adults with a diagnosis of acute bacterial sinusitis (ABS) were evaluated in 3 clinical studies. In one study, 363 patients were randomized to receive either AUGMENTIN XR Extended-Release Tablets 2,000 mg/125 mg orally every 12 hours or levofloxacin 500 mg orally daily for 10 days in a double-blind, multicenter, prospective trial. These patients were clinically and radiologically evaluated at the test of cure (day 17 to 28) visit. The combined clinical and radiological responses were 84% for AUGMENTIN XR Extended-Release Tablets and 84% for levofloxacin at the test of cure visit in clinically evaluable

patients (95% CI for the treatment difference equals -9.4, 8.3). The clinical response rates at the test of cure were 87% and 89%, respectively.

The other 2 trials were non-comparative, multicenter studies designed to assess the bacteriological and clinical efficacy of AUGMENTIN XR Extended-Release Tablets (2,000 mg/125 mg orally every 12 hours for 10 days) in the treatment of 2,288 patients with ABS. Evaluation timepoints were the same as in the prior study. Patients underwent maxillary sinus puncture for culture prior to receiving study medication. Patients with acute bacterial sinusitis due to *S. pneumoniae* with reduced susceptibility to penicillin were accrued through enrollment in these 2 open-label non-comparative clinical trials. Clinical success rates for key pathogens in these studies are shown in Table 15.

Table 15: Clinical Success Rates in Patients with Acute Bacterial Sinusitis

Penicillin MICs of *S. pneumoniae* Isolates	**Intent-To-Treat**			**Clinically Evaluable**		
	n/N[a]	**%**	**95% CI[b]**	**n/N[a]**	**%**	**95% CI[b]**
All *S. pneumoniae*	344/370	93	-	318/326	98	-
MIC greater than or equal to 2.0 mcg/mL[c]	35/36	97	85.5, 99.9	30/31	96	83.3, 99.9
MIC equal to 2.0 mcg/mL	23/24	96	78.9, 99.9	19/20	95	75.1, 99.9
MIC greater than or equal to 4.0 mcg/mL[d]	12/12	100	73.5, 100	11/11	100	71.5, 100
H. influenzae	265/305	87	-	242/259	93	-
M. catarrhalis	94/105	90	-	86/90	96	-

[a]n/N equals patients with pathogen eradicated or presumed eradicated/total number of patients.

[b]Confidence limits calculated using exact probabilities.

[c]*S. pneumoniae* strains with penicillin MICs of greater than or equal to 2 mcg/mL are considered resistant to penicillin.

[d]Includes one patient each with *S. pneumoniae* penicillin MICs of 8 and 16 mcg/mL.

14.5 Acute Bacterial Otitis Media in Pediatric Patients Treated with Amoxicillin and Clavulanate Potassium for Oral Suspension

One randomized, controlled US/Canadian clinical trial evaluated two dosing regimens for amoxicillin and clavulanate potassium for oral suspension in pediatric patients (aged 2 months to 12 years) with acute otitis media. Patients received either 45 mg/6.4 mg/kg/day divided every 12 hours or 40 mg/10 mg/kg/day divided every 8 hours for 10 days. A total of 575 patients were enrolled, with ≥84% evaluable in each group.

Clinical cure rates obtained in the evaluable patients at the end of therapy and follow-up visits are presented in Table 16.

Table 16: Clinical Cure Rates at End of Therapy and Follow-Up Visits

	Amoxicillin and Clavulanate Potassium 45 mg/kg/day, divided every 12 hours	Amoxicillin and Clavulanate Potassium 40 mg/kg/day, divided every 8 hours
Clinical Cure at End of Therapy Visit[a]	87% (n=265)	82% (n=260)
Clinical Cure at Follow-Up Visit	67% (n= 249)	69% (n=243)

[a]Clinical cure at end of therapy visit was defined as 2 to 4 days after the completion of therapy.

[b]Clinical cure at follow-up visit was defined as 22 to 28 days post-completion of therapy.

15 REFERENCES

1. Swanson-Biearman B, Dean BS, Lopez G, Krenzelok EP. The effects of penicillin and cephalosporin ingestions in children less than six years of age. Vet Hum Toxicol. 1988; 30: 66-67.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg per 5 mL is a white to off-white granular powder – Each 5 mL of reconstituted white to pale yellow, orange flavored suspension contains 200 mg of amoxicillin as the trihydrate and 28.5 mg of clavulanic acid as the potassium salt (equivalent to 34 mg of clavulanate potassium).

Bottles of 50 mL NDC 65862-533-50
Bottles of 75 mL NDC 65862-533-75
Bottles of 100 mL NDC 65862-533-01

Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 400 mg/57 mg per 5 mL is a white to off-white granular powder – Each 5 mL of reconstituted white to pale yellow, orange flavored suspension contains 400 mg of amoxicillin as the trihydrate and 57 mg of clavulanic acid as the potassium salt (equivalent to 68 mg of clavulanate potassium).

Bottles of 50 mL NDC 65862-534-50
Bottles of 75 mL NDC 65862-534-75
Bottles of 100 mL NDC 65862-534-01

Storage

Powder for Oral Suspension

Store dry powder at 20º to 25ºC (68º to 77ºF). [See USP Controlled Room Temperature.]

Reconstituted Oral Suspension

Store reconstituted amoxicillin and clavulanate potassium for oral suspension in the original container under refrigeration. Discard unused reconstituted suspension after 10 days. A slight color change during storage is normal. *[see Dosage and Administration (2.7)]*.

17 PATIENT COUNSELING INFORMATION

Administration Instructions

Advise patients or caregivers that when dosing a child with amoxicillin and clavulanate potassium for oral suspension, they should use a dosing spoon or medicine dropper. Be sure to rinse the spoon or dropper after each use *[see Dosage and Administration (2.7)].*

Allergic Reactions

Counsel patients that amoxicillin and clavulanate potassium for oral suspension contains a penicillin class drug product that can cause allergic reactions in some individuals *[see Warnings and Precautions (5.1, 5.3)].*

Severe Cutaneous Adverse Reactions (SCAR)

Advise patients about the signs and symptoms of serious skin manifestations. Instruct patients to stop taking amoxicillin and clavulanate potassium for oral suspension immediately and promptly report the first signs or symptoms of skin rash, mucosal lesions, or any other sign of hypersensitivity *[see Warnings and Precautions (5.2)]*.

Diarrhea

Counsel patients that diarrhea is a common problem caused by antibacterial drugs, including amoxicillin and clavulanate potassium for oral suspension, which usually ends when the antibacterial is discontinued. Sometimes after starting treatment with antibacterial drugs, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as 2 or more months after having taken the last dose of the antibacterial drug. If this occurs, patients should contact their physician as soon as possible. If diarrhea develops and is severe or lasts more than 2 or 3 days, advise the patients to call their doctor *[see Warnings and Precautions (5.5)].*

Risks in Patients with Phenylketonuria

Counsel patients with phenylketonuria that amoxicillin and clavulanate potassium for oral suspension contain aspartame, a source of phenylalanine *[see Warnings and Precautions (5.8)]:*

- Amoxicillin and clavulanate potassium 200 mg/28.5 mg and 400 mg/57 mg for oral suspension contain aspartame. Each 5 mL of the 200 mg/28.5 mg per 5 mL oral suspension contains 4.42 mg phenylalanine and each 5 mL of the 400 mg/57 mg per 5 mL oral suspension contains 6.35 mg phenylalanine.

Antibacterial Resistance

Patients should be counseled that antibacterial drugs, including amoxicillin and clavulanate potassium for oral suspension, should only be used to treat bacterial infections. Antibacterial drugs do not treat viral infections (e.g., the common cold). When amoxicillin and clavulanate potassium for oral suspension is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may: (1) decrease the effectiveness of the immediate treatment, and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by amoxicillin and clavulanate potassium for oral suspension or other antibacterial drugs in the future *[see Warnings and Precautions (5.9)].*

Storage Instructions

Advise patients to keep amoxicillin and clavulanate potassium for oral suspension refrigerated and to shake well before using. Bottles of amoxicillin and clavulanate potassium for oral suspension may contain more liquid than required. Advise patients to follow their doctor’s instructions about the amount to use and the days of treatment required. Discard any unused medicine *[see Dosage and Administration (2.4, 2.7), How Supplied/Storage and Handling (16)].*

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Distributed by:
Aurobindo Pharma USA, Inc.
279 Princeton-Hightstown Road
East Windsor, NJ 08520

Manufactured by:
Aurobindo Pharma Limited
Hyderabad-500 032, India

Revised: 09/2026

PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 200 mg/28.5 mg* per 5 mL (50 mL Bottle Label)

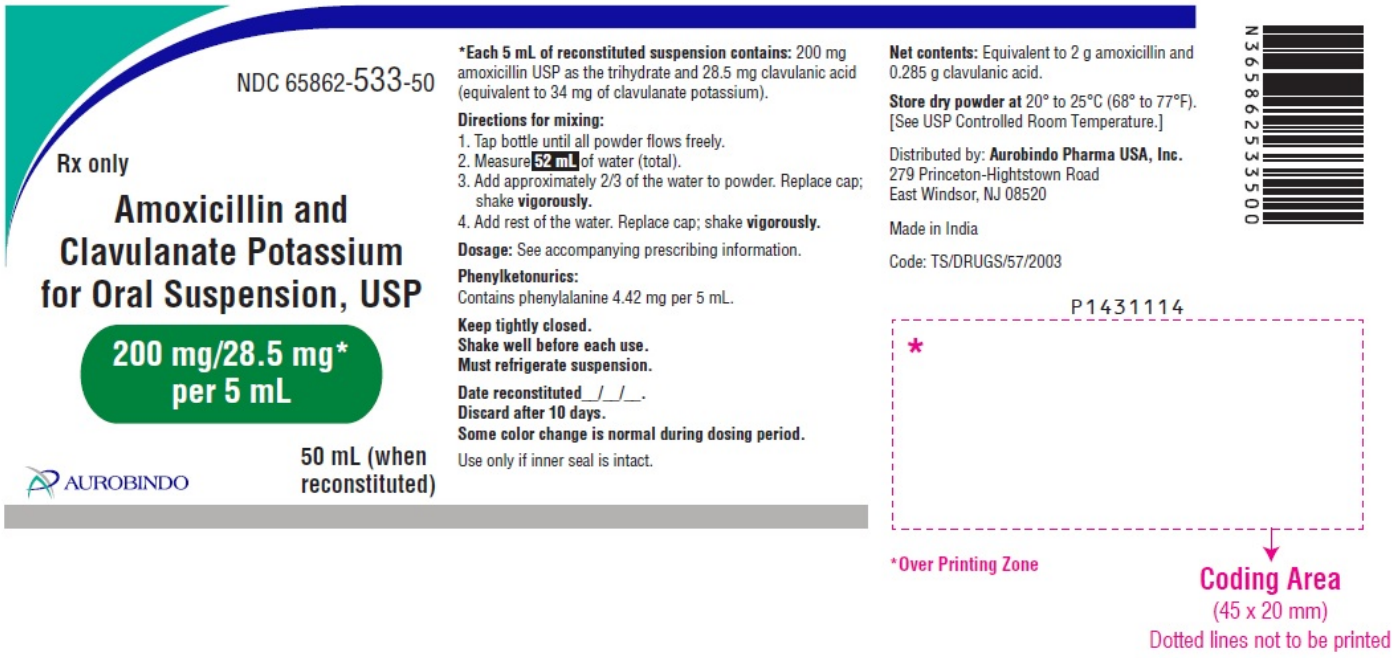
NDC 65862-533-50

Rx only

**Amoxicillin and
Clavulanate Potassium
for Oral Suspension, USP**

**200 mg/28.5 mg*
per 5 mL**

AUROBINDO **50 mL (when reconstituted)**



PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 400 mg/57 mg* per 5 mL (50 mL Bottle Label)

NDC 65862-534-50

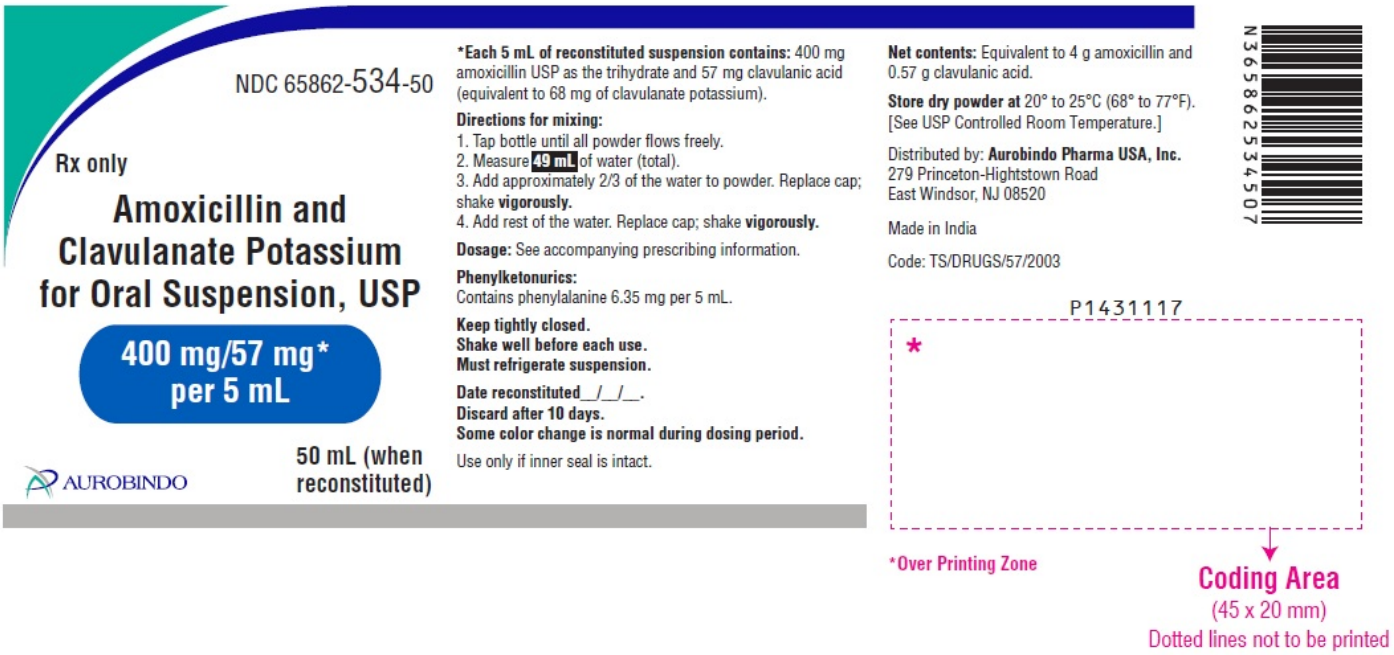
Rx only

**Amoxicillin and
Clavulanate Potassium**

for Oral Suspension, USP

**400 mg/57 mg*
per 5 mL**

AUROBINDO **50 mL (when reconstituted)**



AMOXICILLIN AND CLAVULANATE POTASSIUM

amoxicillin and clavulanate potassium powder, for suspension

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:65862-533
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
AMOXICILLIN (UNII: 804826J2HU) (AMOXICILLIN ANHYDROUS - UNII:9EM05410Q9)	AMOXICILLIN ANHYDROUS	200 mg in 5 mL
CLAVULANATE POTASSIUM (UNII: Q42OMW3AT8) (CLAVULANIC ACID - UNII:23521W1S24)	CLAVULANIC ACID	28.5 mg in 5 mL

Inactive Ingredients	
Ingredient Name	**Strength**
ASPARTAME (UNII: Z0H242BBR1)	
HYPROMELLOSE 2910 (50 MPA.S) (UNII: 1IVH67816N)	

ORANGE (UNII: 5EVU04N5QU)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
SUCCINIC ACID (UNII: AB6MNQ6J6L)	
XANTHAN GUM (UNII: TTV12P4NEE)	

Product Characteristics			
Color	WHITE (White to Off-white)	**Score**	
Shape		**Size**	
Flavor	ORANGE	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:65862-533-50	50 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/20/2011	
2	NDC:65862-533-75	75 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/20/2011	
3	NDC:65862-533-01	100 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/20/2011	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA201090	12/20/2011	

AMOXICILLIN AND CLAVULANATE POTASSIUM

amoxicillin and clavulanate potassium powder, for suspension

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:65862-534
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMOXICILLIN (UNII: 804826J2HU) (AMOXICILLIN ANHYDROUS - UNII:9EM05410Q9)	AMOXICILLIN ANHYDROUS	400 mg in 5 mL
CLAVULANATE POTASSIUM (UNII: Q42OMW3AT8) (CLAVULANIC ACID - UNII:23521W1S24)	CLAVULANIC ACID	57 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength

ASPARTAME (UNII: Z0H242BBR1)	
HYPROMELLOSE 2910 (50 MPA.S) (UNII: 1IVH67816N)	
ORANGE (UNII: 5EVU04N5QU)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
SUCCINIC ACID (UNII: AB6MNQ6J6L)	
XANTHAN GUM (UNII: TTV12P4NEE)	

Product Characteristics

Color	WHITE (White to Off-white)	**Score**	
Shape		**Size**	
Flavor	ORANGE	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:65862-534-50	50 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/20/2011	
2	NDC:65862-534-75	75 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/20/2011	
3	NDC:65862-534-01	100 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/20/2011	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA201090	12/20/2011	

Labeler - Aurobindo Pharma Limited (650082092)

Establishment

Name	Address	ID/FEI	Business Operations
Aurobindo Pharma Limited		918917683	ANALYSIS(65862-533, 65862-534) , MANUFACTURE(65862-533, 65862-534)

Revised: 9/2026 Aurobindo Pharma Limited