

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TIMENTIN safely and effectively. See full prescribing information for TIMENTIN.

**TIMENTIN® (ticarcillin disodium and clavulanate potassium) for Injection**

**TIMENTIN® (ticarcillin disodium and clavulanate potassium) for Injection: Pharmacy Bulk Package**

**TIMENTIN® (ticarcillin disodium and clavulanate potassium) Injection: GALAXY**

Initial U.S. Approval: 1985

To reduce the development of drug-resistant bacteria and maintain the effectiveness of TIMENTIN and other antibacterial drugs, TIMENTIN should be used only to treat infections that are proven or strongly suspected to be caused by bacteria.

### INDICATIONS AND USAGE

TIMENTIN is a combination of a  $\beta$ -lactam antibacterial and a  $\beta$ -lactamase inhibitor indicated for the treatment of the following infections due to designated susceptible bacteria:

- Septicemia (1.1)
- Lower respiratory-infections (1.2)
- Bone and joint infections (1.3)
- Skin and skin structure infections (1.4)
- Urinary tract infections (1.5)
- Gynecologic infections (1.6)
- Intra-abdominal infections (1.7)

### DOSAGE AND ADMINISTRATION

Administer TIMENTIN by intravenous infusion (30 minutes). (2)

Adults:

- Systemic and urinary tract infections: 3.1 g every 4 to 6 hours.
- Gynecologic infections: 200 to 300 mg/kg/day in divided doses every 4 to 6 hours depending on severity of infection. (2.1)

Pediatric Patients:

- <60 kg: 200 to 300 mg/kg/day in divided doses every 4 to 6 hours depending on severity of infection. (2.2)
- $\geq$ 60 kg: 3.1 grams every 4 to 6 hours depending on severity of infection. (2.2)

### DOSAGE FORMS AND STRENGTHS

- 3.1 gram vial of TIMENTIN for Injection containing ticarcillin disodium equivalent to 3 grams ticarcillin and clavulanate potassium equivalent to 0.1 gram clavulanic acid. (3)

- 31-gram Pharmacy Bulk Package of TIMENTIN for Injection containing ticarcillin disodium equivalent to 30 grams ticarcillin and clavulanate potassium equivalent to 1 gram clavulanic acid. (3)
- 100-mL single-dose GALAXY (PL 2040) Plastic bag of TIMENTIN Injection in containing ticarcillin disodium equivalent to 3.0 grams ticarcillin and clavulanate potassium equivalent to 0.1 gram clavulanic acid as a frozen solution (3)

### CONTRAINDICATIONS

History of a serious hypersensitivity reaction (anaphylaxis or Stevens-Johnson syndrome) to TIMENTIN or to other  $\beta$ -lactams (e.g., penicillins and cephalosporins). (4)

### WARNINGS AND PRECAUTIONS

- Serious hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Discontinue TIMENTIN and institute appropriate therapy. (5.1)
- *Clostridium difficile* associated diarrhea (CDAD) has been reported with nearly all systemic antibacterial agents: If diarrhea occurs, evaluate patients for CDAD. (5.2)
- Convulsions: Patients may experience convulsions when the dose of TIMENTIN exceeds the recommended dose, especially in the presence of impaired renal function.(5.3).

### ADVERSE REACTIONS

Most common adverse reactions ( $\geq$ 1%) are rash, nausea, diarrhea, and phlebitis at injection site. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

- Aminoglycosides: Mixing with TIMENTIN for parenteral administration can inactivate the aminoglycoside. (7.1)
- Probenecid: Interferes with renal tubular secretion of ticarcillin, therefore increases exposure to ticarcillin. (7.2)
- Oral Contraceptives: Effects on gut flora may lower estrogen reabsorption and reduce efficacy of oral contraceptives. (7.3)

### USE IN SPECIFIC POPULATIONS

Renal Impairment: Adjust dose based on creatinine clearance and type of dialysis. (2.3, 8.6)

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Revised: Month Year

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1 **FULL PRESCRIBING INFORMATION**

2 **1 INDICATIONS AND USAGE**

3 TIMENTIN<sup>®</sup> is indicated in the treatment of infections caused by susceptible isolates of  
4 the designated bacteria in the conditions listed below:

5 **1.1 Septicemia**

6 Septicemia (including bacteremia) caused by  $\beta$ -lactamase-producing isolates of  
7 *Klebsiella* spp. \*, *Escherichia coli* \*, *Staphylococcus aureus* \*, or *Pseudomonas aeruginosa* \* (or  
8 other *Pseudomonas* species \*)

9 **1.2 Lower Respiratory Infections**

10 Lower respiratory infections caused by  $\beta$ -lactamase-producing isolates of *S. aureus*,  
11 *Haemophilus influenzae* \*, or *Klebsiella* spp.\*

12 **1.3 Bone and Joint Infections**

13 Bone and joint infections caused by  $\beta$ -lactamase-producing isolates of *S. aureus*

14 **1.4 Skin and Skin Structure Infections**

15 Skin and skin structure infections caused by  $\beta$ -lactamase-producing isolates of *S. aureus*,  
16 *Klebsiella* spp. \*, or *E. coli* \*

17 **1.5 Urinary Tract Infections**

18 Urinary tract infections (complicated and uncomplicated) caused by  $\beta$ -lactamase-  
19 producing isolates of *E. coli*, *Klebsiella* spp., *P. aeruginosa* \* (or other *Pseudomonas* spp.\*),  
20 *Citrobacter* spp. \*, *Enterobacter cloacae* \*, *Serratia marcescens* \*, or *S. aureus* \*

21 **1.6 Gynecologic Infections**

22 Endometritis caused by  $\beta$ -lactamase-producing isolates of *Prevotella melaninogenicus* \*,  
23 *Enterobacter* spp. (including *E. cloacae* \*), *E. coli*, *Klebsiella pneumoniae* \*, *S. aureus*, or  
24 *Staphylococcus epidermidis*

25 **1.7 Intra-abdominal Infections**

26 Peritonitis caused by  $\beta$ -lactamase-producing isolates of *E. coli*, *K. pneumoniae*, or  
27 *Bacteroides fragilis* \* group

28 \*Efficacy for this organism in this organ system was studied in fewer than 10 infections.

29 To reduce the development of drug-resistant bacteria and maintain the effectiveness of  
30 TIMENTIN and other antibacterial drugs, TIMENTIN should be used only to treat infections  
31 that are proven or strongly suspected to be caused by susceptible bacteria. When culture and  
32 susceptibility information are available, they should be considered in selecting or modifying  
33 antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns  
34 may contribute to the empiric selection of therapy.

35 **2 DOSAGE AND ADMINISTRATION**

36 **2.1 Adults**

37 The usual recommended dosage for systemic and urinary tract infections for adults is  
38 3.1 grams of TIMENTIN (3 grams ticarcillin and 100 mg clavulanic acid) given every 4 to  
39 6 hours. For gynecologic infections, TIMENTIN should be administered as follows (based on  
40 ticarcillin content): Moderate infections, 200 mg/kg/day in divided doses every 6 hours; Severe  
41 infections, 300 mg/kg/day in divided doses every 4 hours. For patients weighing less than 60 kg,  
42 the recommended dosage is 200 to 300 mg/kg/day given in divided doses every 4 to 6 hours.

43 The duration of therapy depends upon the severity of infection. The usual duration is 10  
44 to 14 days; however, in difficult and complicated infections, more prolonged therapy may be  
45 required.

46 **2.2 Pediatric Patients (≥3 Months)**

47 Patients <60 kg: Mild to moderate infections, 200 mg/kg/day based on ticarcillin content  
48 in divided doses every 6 hours; Severe infections, 300 mg/kg/day in divided doses every 4 hours.

49 Patients ≥60 kg: Mild to moderate infections, 3.1 grams every 6 hours; Severe infections,  
50 3.1 grams every 4 hours.

51 **2.3 Renal Impairment**

52 For patients with renal insufficiency, an initial loading dose of 3.1 grams should be  
53 followed by doses based on creatinine clearance and type of dialysis as indicated in Table 1.  
54

55 **Table 1. Dosage Adjustments for Renal Impairment**

Creatinine Clearance (mL/minute) <sup>a</sup>	Dosage <sup>b</sup>
Over 60	3 grams every 4 hours
30 to 60	2 grams every 4 hours
10 to 30	2 grams every 8 hours
Less than 10	2 grams every 12 hours
Less than 10 with hepatic dysfunction	2 grams every 24 hours
Patients on peritoneal dialysis	3 grams every 12 hours
Patients on hemodialysis	2 grams every 12 hours supplemented with 3 grams after each dialysis

56 <sup>a</sup> To calculate creatinine clearance<sup>1</sup> from a serum creatinine value use the following formula:

57 
$$C_{cr} = (140 - \text{Age}) (\text{weight in kg}) / 72 \times S_{cr} (\text{mg}/100 \text{ mL})$$

58 This is the calculated creatinine clearance for adult males; for females it is 15% less.

59 <sup>b</sup> Based on ticarcillin content.  
60

61 **2.4 Administration and Directions for Use**

62 TIMENTIN should be administered by intravenous infusion over a 30-minute period.

63 Directions for Reconstitution and Further Dilution: *3.1-gram Glass Vials:* The 3.1-gram  
64 vial should be reconstituted by adding approximately 13 mL of Sterile Water for Injection, USP,  
65 or Sodium Chloride Injection, USP, and shaking well. When dissolved, the concentration of

66 ticarcillin will be approximately 200 mg/mL with a corresponding concentration of 6.7 mg/mL  
67 for clavulanic acid. The color of reconstituted solutions of TIMENTIN normally ranges from  
68 light to dark yellow, depending on concentration, duration, and temperature of storage.

69 The dissolved drug should be further diluted to desired volume using the recommended  
70 solution listed under Stability below [*see Dosage and Administration (2.5)*] to a concentration  
71 between 10 mg/mL to 100 mg/mL.

72 *Pharmacy Bulk Package:* The container closure may be penetrated only one time  
73 utilizing a suitable sterile transfer device or dispensing set that allows measured distribution of  
74 the contents. A sterile substance that must be reconstituted prior to use may require a separate  
75 closure entry.

76 Restrict use of Pharmacy Bulk Packages to an aseptic area such as a laminar flow hood.  
77 Reconstituted contents of the vial should be withdrawn immediately. However, if this is  
78 not possible, aliquoting operations must be completed within 4 hours of reconstitution. Discard  
79 the reconstituted stock solution 4 hours after initial entry.

80 Add 76 mL of Sterile Water for Injection, USP, or Sodium Chloride Injection, USP, to  
81 the 31-gram Pharmacy Bulk Package and shake well. For ease of reconstitution, the diluent may  
82 be added in 2 portions. Each 1 mL of the resulting concentrated stock solution contains  
83 approximately 300 mg of ticarcillin and 10 mg of clavulanic acid.

84 The desired dosage should be withdrawn from the stock solution and further diluted to  
85 desired volume using the recommended solution listed under Stability below [*see Dosage and*  
86 *Administration (2.5)*] to a concentration between 10 mg/mL to 100 mg/mL.

87 Directions for Intravenous Infusion: After reconstitution and further dilution and prior to  
88 administration, TIMENTIN should be inspected visually for particulate matter. If particulate  
89 matter is present, the solution should be discarded.

90 The solution of reconstituted drug may be administered over a 30-minute period by direct  
91 infusion or through a Y-type intravenous infusion set. If this method of administration is used, it  
92 is advisable to temporarily discontinue the administration of any other solutions during the  
93 infusion of TIMENTIN.

94 When TIMENTIN is given in combination with another antimicrobial, such as an  
95 aminoglycoside, each drug should be given separately in accordance with the recommended  
96 dosage and routes of administration for each drug. [*See Drug Interactions (7.1).*]

97 ***GALAXY Container:*** Prior to administration, TIMENTIN should be inspected  
98 visually for particulate matter. If particulate matter is present, the solution should be discarded.

99 Caution: Do not use plastic containers in series connections. Such use could result in an  
100 embolism due to residual air being drawn from the primary container before administration of  
101 the fluid from the secondary container is completed.

102 Preparation for Administration: See How Supplied/Storage and Handling (16) for  
103 thawing and handling instructions:

- 104 • Suspend the container from eyelet support.
- 105 • Remove protector from outlet port at bottom of container.

106 • Attach administration set. Refer to complete directions accompanying set.

107 **2.5 Stability**

108 **NOTE:** TIMENTIN is incompatible with Sodium Bicarbonate.

109 3.1-gram Glass Vials: The concentrated stock solution at 200 mg/mL is stable for up to  
110 6 hours at room temperature 21° to 24°C (70° to 75°F) or up to 72 hours under refrigeration 4°C  
111 (40°F).

112 If the concentrated stock solution (200 mg/mL) is held for up to 6 hours at room  
113 temperature 21° to 24°C (70° to 75°F) or up to 72 hours under refrigeration 4°C (40°F) and  
114 further diluted to a concentration between 10 mg/mL and 100 mg/mL with any of the diluents  
115 listed below, then the following stability periods apply.

116

<b>STABILITY PERIOD</b>		
<b>(3.1-gram Vials)</b>		
<b>Intravenous Solution (ticarcillin concentrations of 10 mg/mL to 100 mg/mL)</b>	<b>Room Temperature 21° to 24°C (70° to 75°F)</b>	<b>Refrigerated 4°C (40°F)</b>
Dextrose Injection 5%, USP	24 hours	3 days
Sodium Chloride Injection, USP	24 hours	7 days
Lactated Ringer's Injection, USP	24 hours	7 days

117

118 If the concentrated stock solution (200 mg/mL) is stored for up to 6 hours at room  
119 temperature and then further diluted to a concentration between 10 mg/mL and 100 mg/mL,  
120 solutions of Sodium Chloride Injection, USP, and Lactated Ringer's Injection, USP, may be  
121 stored frozen -18°C (0°F) for up to 30 days. Solutions prepared with Dextrose Injection 5%,  
122 USP, may be stored frozen -18°C (0°F) for up to 7 days. All thawed solutions should be used  
123 within 8 hours or discarded. Once thawed, solutions should not be refrozen.

124 Unused solutions must be discarded after the time periods listed above.

125 Pharmacy Bulk Package: Aliquots of the reconstituted stock solution at 300 mg/mL are  
126 stable for up to 6 hours between 21° and 24°C (70° and 75°F) or up to 72 hours under  
127 refrigeration 4°C (40°F). The reconstituted stock solution should be held under refrigeration 4°C  
128 (40°F).

129 If the aliquots of the reconstituted stock solution (300 mg/mL) are held up to 6 hours  
130 between 21° and 24°C (70° and 75°F) or up to 72 hours under refrigeration 4°C (40°F) and  
131 further diluted to a concentration between 10 mg/mL and 100 mg/mL with any of the diluents  
132 listed below, then the following stability periods apply.

133

<b>STABILITY PERIOD</b>		
<b>(31-gram Pharmacy Bulk Package)</b>		
<b>Intravenous Solution (ticarcillin concentrations of 10 mg/mL to 100 mg/mL)</b>	<b>Room Temperature 21° to 24°C (70° to 75°F)</b>	<b>Refrigerated 4°C (40°F)</b>
Dextrose Injection 5%, USP	24 hours	3 days
Sodium Chloride Injection 0.9%, USP	24 hours	4 days
Lactated Ringer's Injection, USP	24 hours	4 days
Sterile Water for Injection, USP	24 hours	4 days

134  
135 If an aliquot of concentrated stock solution (300 mg/mL) is stored for up to 6 hours  
136 between 21° and 24°C (70° and 75°F) and then further diluted to a concentration between  
137 10 mg/mL and 100 mg/mL, solutions of Sodium Chloride Injection, USP, Lactated Ringer's  
138 Injection, USP, and Sterile Water for Injection, USP, may be stored frozen –18°C (0°F) for up to  
139 30 days. Solutions prepared with Dextrose Injection 5%, USP, may be stored frozen –18°C (0°F)  
140 for up to 7 days. All thawed solutions should be used within 8 hours or discarded. Once thawed,  
141 solutions should not be refrozen.

142 Unused solutions must be discarded after the time periods listed above.

143 GALAXY containers: Do not add supplementary medication to the bag. The thawed  
144 solution is stable for 24 hours at room temperature 22°C (72°F) or for 7 days under refrigeration  
145 at 4°C (39°F)

### 146 **3 DOSAGE FORMS AND STRENGTHS**

147 The 3.1-gram glass vial of TIMENTIN for Injection is a white to pale yellow sterile  
148 powder for reconstitution containing ticarcillin disodium equivalent to 3 grams ticarcillin and  
149 clavulanate potassium equivalent to 0.1 gram clavulanic acid.

150 The 31-gram Pharmacy Bulk Package of TIMENTIN for Injection is a white to pale  
151 yellow sterile powder for reconstitution containing ticarcillin disodium equivalent to 30 grams  
152 ticarcillin and clavulanate potassium equivalent to 1 gram clavulanic acid.

153 The 100-mL single-dose GALAXY® Plastic Container of TIMENTIN is a frozen solution  
154 containing ticarcillin disodium equivalent to 3.0 grams ticarcillin and clavulanate potassium  
155 equivalent to 0.1 gram clavulanic acid.

### 156 **4 CONTRAINDICATIONS**

157 TIMENTIN is contraindicated in patients who have a history of hypersensitivity reaction  
158 (e.g., anaphylaxis or erythema multiforme) to TIMENTIN or to other β-lactam antibacterials  
159 (e.g., penicillins and cephalosporins).

160 **5 WARNINGS AND PRECAUTIONS**

161 **5.1 Anaphylactic Reactions**

162 Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been  
163 reported in patients on penicillin therapy. These reactions are more likely to occur in individuals  
164 with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens.  
165 There have been reports of individuals with a history of penicillin hypersensitivity who have  
166 experienced severe reactions when treated with cephalosporins. Before initiating therapy with  
167 TIMENTIN, careful inquiry should be made regarding previous hypersensitivity reactions to  
168 penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, TIMENTIN should  
169 be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions require  
170 immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway  
171 management, including intubation, should also be provided as indicated.

172 **5.2 *Clostridium difficile* Associated Diarrhea**

173 *Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all  
174 antibacterial agents, including TIMENTIN, and may range in severity from mild diarrhea to fatal  
175 colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to  
176 overgrowth of *C. difficile*.

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

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

187 **5.3 Convulsions**

188 Patients may experience convulsions when the dose of TIMENTIN exceeds the  
189 recommended dose, especially in the presence of impaired renal function [*see Adverse Reactions*  
190 (6.2) and *Overdosage (10)*].

191 **5.4 Risk of Bleeding**

192 Some patients receiving  $\beta$ -lactam antibacterials have experienced bleeding associated  
193 with abnormalities in coagulation tests. These adverse reactions are more likely to occur in  
194 patients with renal impairment. If bleeding manifestations appear, treatment with TIMENTIN  
195 should be discontinued and appropriate therapy instituted.

196 **5.5 Potential for Microbial Overgrowth or Bacterial Resistance**

197 The possibility of superinfections with fungal or bacterial pathogens should be  
198 considered during therapy. If superinfections occur, appropriate measures should be taken.

199 Prescribing TIMENTIN either in the absence of a proven or strongly suspected bacterial  
200 infection is unlikely to provide benefit to the patient and increases the risk of the development of  
201 drug-resistant bacteria.

## 202 **5.6 Interference with Laboratory Tests**

203 High urine concentrations of ticarcillin may produce false-positive protein reactions  
204 (pseudoproteinuria) [see *Drug Interactions (7.4)*].

205 Clavulanic acid may cause a nonspecific binding of IgG and albumin by red cell  
206 membranes, leading to a false-positive Coombs test [see *Drug Interactions (7.4)*].

## 207 **5.7 Electrolyte Imbalance**

208 Hypokalemia has been reported during treatment with TIMENTIN. Serum potassium  
209 should be monitored in patients with fluid and electrolyte imbalance and in patients receiving  
210 prolonged therapy. The theoretical sodium content is 4.51 mEq (103.6 mg) per gram of  
211 TIMENTIN. This should be considered when treating patients requiring restricted salt intake.

## 212 **6 ADVERSE REACTIONS**

213 The following are discussed in more detail in other sections of the labeling:

- 214 • Anaphylactic Reactions [see *Warnings and Precautions (5.1)*]
- 215 • *Clostridium difficile* Associated Diarrhea [see *Warnings and Precautions (5.2)*]

### 216 **6.1 Clinical Trials Experience**

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

220 Adverse reactions occurring in  $\geq 1\%$  of 867 patients receiving TIMENTIN 3.1 grams in  
221 clinical studies included rash, nausea, diarrhea, and phlebitis at the injection site. The most  
222 common laboratory abnormalities ( $\geq 3\%$ ) were elevations in eosinophils, serum aspartate  
223 aminotransferase (AST), and serum alanine aminotransferase (ALT).

224 Available safety data for pediatric patients treated with TIMENTIN demonstrate a similar  
225 adverse event profile to that observed in adult patients.

### 226 **6.2 Postmarketing Experience**

227 In addition to adverse reactions reported from clinical trials, the following adverse  
228 reactions have been identified during post-marketing use of TIMENTIN. Because they are  
229 reported voluntarily from a population of unknown size, estimates of frequency cannot be made.  
230 These adverse reactions have been chosen for inclusion due to a combination of their  
231 seriousness, frequency of reporting, or potential causal connection to TIMENTIN.

232 Hypersensitivity Reactions: Skin rash, pruritus, urticaria, arthralgia, myalgia, drug fever,  
233 chills, chest discomfort, anaphylactic reactions, and bullous reactions (including erythema  
234 multiforme, toxic epidermal necrolysis, and Stevens-Johnson syndrome).

235 Central Nervous System: Headache, giddiness, neuromuscular hyperirritability, or  
236 convulsive seizures.

237 Gastrointestinal Disturbances: Disturbances of taste and smell, stomatitis, flatulence,  
238 nausea, vomiting and diarrhea, epigastric pain, and pseudomembranous colitis have been  
239 reported. Onset of pseudomembranous colitis symptoms may occur during or after antibacterial  
240 treatment [see *Warnings and Precautions (5.2)*].

241 Hemic and Lymphatic Systems: Thrombocytopenia, leukopenia, neutropenia,  
242 eosinophilia, reduction of hemoglobin or hematocrit, and prolongation of prothrombin time and  
243 bleeding time.

244 Abnormalities of Hepatic Function Tests: Elevation of AST, ALT, serum alkaline  
245 phosphatase, serum LDH, and serum bilirubin. There have been reports of transient hepatitis and  
246 cholestatic jaundice, as with some other penicillins and some cephalosporins.

247 Renal and Urinary Effects: Hemorrhagic cystitis, elevation of serum creatinine and/or  
248 BUN, hypernatremia, reduction in serum potassium, and uric acid.

249 Local Reactions: Pain, burning, swelling, and induration at the injection site and  
250 thrombophlebitis with intravenous administration.

## 251 **7 DRUG INTERACTIONS**

### 252 **7.1 Aminoglycosides**

253 The mixing of TIMENTIN with an aminoglycoside in solutions for parenteral  
254 administration can result in substantial inactivation of the aminoglycoside.

### 255 **7.2 Probenecid**

256 Probenecid interferes with the renal tubular secretion of ticarcillin, thereby increasing  
257 serum concentrations and prolonging serum half-life of ticarcillin. Probenecid does not affect the  
258 serum levels of clavulanic acid.

### 259 **7.3 Oral Contraceptives**

260 Ticarcillin disodium/clavulanate potassium may affect the gut flora, leading to lower  
261 estrogen reabsorption and reduced efficacy of combined oral estrogen/progesterone  
262 contraceptives.

### 263 **7.4 Effects on Laboratory Tests**

264 High urine concentrations of ticarcillin may produce false-positive protein reactions  
265 (pseudoproteinuria) with certain methods. The bromphenol blue reagent strip test has been  
266 reported to be a reliable method for testing protein reactions [see *Warnings and Precautions*  
267 (5.6)].

268 Clavulanic acid in TIMENTIN may cause a nonspecific binding of IgG and albumin by  
269 red cell membranes, leading to a false-positive Coombs test. A positive Coombs test should be  
270 interpreted with caution during TIMENTIN treatment [see *Warnings and Precautions (5.6)*].

## 271 **8 USE IN SPECIFIC POPULATIONS**

### 272 **8.1 Pregnancy**

273 Teratogenic Effects: Pregnancy Category B: Reproduction studies have been performed  
274 in rats given doses up to 1,050 mg/kg/day (approximately half of the recommended human dose  
275 on a body surface area basis) and have revealed no evidence of impaired fertility or harm to the

276 fetus due to TIMENTIN. There are, however, no adequate and well-controlled studies in  
277 pregnant women. Because animal reproduction studies are not always predictive of human  
278 response, this drug should be used during pregnancy only if clearly needed.

### 279 **8.3 Nursing Mothers**

280 It is not known whether ticarcillin or clavulanic acid is excreted in human milk. Because  
281 many drugs are excreted in human milk, caution should be exercised when TIMENTIN is  
282 administered to a nursing woman.

### 283 **8.4 Pediatric Use**

284 The safety and effectiveness of TIMENTIN have been established in the age group of  
285 3 months to 16 years. Use of TIMENTIN in these age groups is supported by evidence from  
286 adequate and well-controlled studies of TIMENTIN in adults with additional efficacy, safety,  
287 and pharmacokinetic data from both comparative and non-comparative studies in pediatric  
288 patients. There are insufficient data to support the use of TIMENTIN in pediatric patients under  
289 3 months of age.

290 If meningitis is suspected or documented, an alternative agent with demonstrated clinical  
291 efficacy in this setting should be used.

### 292 **8.5 Geriatric Use**

293 An analysis of clinical studies of TIMENTIN was conducted to determine whether  
294 subjects aged 65 and over respond differently from younger subjects. Of the 1,078 subjects  
295 treated with at least one dose of TIMENTIN, 67.5% were <65 years old, and 32.5% were  
296 ≥65 years old. No overall differences in safety or efficacy were observed between older and  
297 younger subjects, and other reported clinical experience have not identified differences in  
298 responses between the elderly and younger patients, but a greater sensitivity of some older  
299 individuals cannot be ruled out.

300 This drug is known to be substantially excreted by the kidney, and the risk of toxic  
301 reactions to this drug may be greater in patients with impaired renal function. Because elderly  
302 patients are more likely to have decreased renal function, care should be taken in dose selection,  
303 and it may be useful to monitor renal function [*see Dosage and Administration (2.3)*].

304 TIMENTIN contains 103.6 mg (4.51 mEq) of sodium per gram of TIMENTIN. At the  
305 usual recommended doses, patients would receive between 1,285 and 1,927 mg/day (56 and  
306 84 mEq) of sodium. The geriatric population may respond with a blunted natriuresis to salt  
307 loading. This may be clinically important with regard to such diseases as congestive heart failure.

### 308 **8.6 Renal Impairment**

309 Ticarcillin is predominantly excreted by the kidney [*see Clinical Pharmacology (12.3)*].  
310 Dosage adjustments should be made for patients with renal impairment [*see Dosage and*  
311 *Administration (2.3)*].

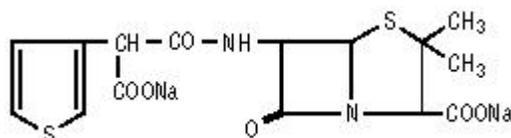
312 **10 OVERDOSAGE**

313 In case of overdose, discontinue TIMENTIN, treat symptomatically, and institute  
314 supportive measures as required. Ticarcillin and clavulanic acid may be removed from  
315 circulation by hemodialysis.

316 **11 DESCRIPTION**

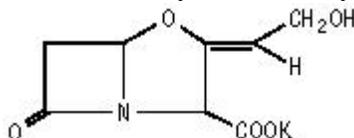
317 TIMENTIN (ticarcillin disodium and clavulanate potassium) for Injection,  
318 3.1-gram glass vial, 31-gram Pharmacy Bulk Package, and TIMENTIN (ticarcillin disodium and  
319 clavulanate potassium) Injection in the GALAXY bag are a combination of ticarcillin disodium  
320 and the  $\beta$ -lactamase inhibitor clavulanate potassium (the potassium salt of clavulanic acid) for  
321 intravenous administration. Ticarcillin is derived from the basic penicillin nucleus,  
322 6-amino-penicillanic acid.

323 Chemically, ticarcillin disodium is *N*-(2-Carboxy-3,3-dimethyl-7-oxo-4-thia-1-  
324 azabicyclo[3.2.0]hept-6-yl)-3-thiophenemalonamic acid disodium salt and may be represented  
325 as:



326  
327 Clavulanic acid is produced by the fermentation of *Streptomyces clavuligerus*. It is a  
328  $\beta$ -lactam structurally related to the penicillins and possesses the ability to inactivate a wide  
329 variety of  $\beta$ -lactamases by blocking the active sites of these enzymes. Clavulanic acid is  
330 particularly active against the clinically important plasmid-mediated  $\beta$ -lactamases frequently  
331 responsible for transferred drug resistance to penicillins and cephalosporins.

332 Chemically, clavulanate potassium is potassium (*Z*)-(2*R*,5*R*)-3-(2-hydroxyethylidene)-7-  
333 oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylate and may be represented structurally as:



334  
335 TIMENTIN (ticarcillin disodium and clavulanate potassium) for Injection, the 3.1-gram  
336 glass vial or the 31-gram Pharmacy Bulk Package, are white to pale yellow sterile powders to be  
337 reconstituted and diluted for intravenous infusion. The reconstituted solution is clear, colorless or  
338 pale yellow, with a pH of 5.5 to 7.5. The 3.1-gram glass vial of TIMENTIN for Injection  
339 contains ticarcillin disodium equivalent to 3 grams ticarcillin and clavulanate potassium  
340 equivalent to 0.1 gram clavulanic acid. The 31-gram TIMENTIN for Injection Pharmacy Bulk  
341 Package contains ticarcillin disodium equivalent to 30 grams ticarcillin and clavulanate  
342 potassium equivalent to 1 gram clavulanic acid.

343 TIMENTIN (ticarcillin disodium and clavulanate potassium) Injection in GALAXY bag  
344 is an iso-osmotic, sterile, nonpyrogenic, frozen solution containing 3.0 grams ticarcillin as  
345 ticarcillin disodium and 0.1 gram clavulanic acid as clavulanate potassium and approximately

346 0.3 gram sodium citrate hydrous as a buffer. The solution is intended for intravenous use after  
347 thawing to room temperature. The pH of thawed solution ranges from 5.5 to 7.5.

348 For the 3.1 gram dosage of TIMENTIN, the theoretical sodium content is 4.51 mEq  
349 (103.6 mg) per gram of TIMENTIN. The theoretical potassium content is 0.15 mEq (6 mg) per  
350 gram of TIMENTIN.

## 351 12 CLINICAL PHARMACOLOGY

### 352 12.1 Mechanism of Action

353 TIMENTIN is an antibacterial drug [see Microbiology (12.4)].

### 354 12.3 Pharmacokinetics

355 After an intravenous infusion (30 minutes) of 3.1 grams of TIMENTIN, peak serum  
356 concentrations of both ticarcillin and clavulanic acid were attained immediately after completion  
357 of the infusion. Ticarcillin serum levels were similar to those produced by the administration of  
358 equivalent amounts of ticarcillin alone with a mean peak serum level of 324 mcg/mL. The  
359 corresponding mean peak serum level for clavulanic acid was 8 mcg/mL. (See Table 2.)  
360

361 **Table 2. Mean Peak Serum Levels (mcg/mL) in Adults after a 30-Minute IV Infusion of**  
362 **3.1 gram of TIMENTIN**

Time	Ticarcillin Peak (Range)	Clavulanic Acid Peak (Range)
0	324 (293-388)	8.0 (5.3-10.3)
15 minutes	223 (184-293)	4.6 (3.0-7.6)
30 minutes	176 (135-235)	2.6 (1.8-3.4)
1 hour	131 (102-195)	1.8 (1.6-2.2)
1.5 hours	90 (65-119)	1.2 (0.8-1.6)
3.5 hours	27 (19-37)	0.3 (0.2-0.3)
5.5 hours	6 (5-7)	0

363  
364 The mean area under the serum concentration curve was 485 mcg•hr/mL for ticarcillin  
365 and 8.2 mcg•hr/mL for clavulanic acid.

366 Distribution: Ticarcillin has been found to be approximately 45% bound to human serum  
367 protein and clavulanic acid approximately 25% bound. Ticarcillin can be detected in tissues and  
368 interstitial fluid following parenteral administration.

369 Distribution of ticarcillin into bile and pleural fluid has been demonstrated. The results of  
370 experiments involving the administration of clavulanic acid to animals suggest that this  
371 compound, like ticarcillin, is well distributed in body tissues.

372 Elimination: Approximately 60% to 70% of ticarcillin and approximately 35% to 45% of  
373 clavulanic acid are excreted unchanged in urine during the first 6 hours after administration of a  
374 single dose of TIMENTIN to normal volunteers with normal renal function. Two hours after an  
375 intravenous injection of 3.1 grams of TIMENTIN, concentrations of ticarcillin in urine generally  
376 exceed 1,500 mcg/mL. The corresponding concentrations of clavulanic acid in urine generally

377 exceed 40 mcg/mL. By 4 to 6 hours after injection, the urine concentrations of ticarcillin and  
378 clavulanic acid usually decline to approximately 190 mcg/mL and 2 mcg/mL, respectively.

379 The mean serum half-life of both ticarcillin and clavulanic acid in healthy volunteers was  
380 1.1 hours.

381 Pediatrics: In pediatric patients receiving approximately 50 mg/kg of TIMENTIN (30:1  
382 ratio ticarcillin to clavulanate), mean ticarcillin serum half-lives were 4.4 hours in neonates  
383 (n = 18) and 1.0 hour in infants and children (n = 41). The corresponding clavulanate serum  
384 half-lives averaged 1.9 hours in neonates (n = 14) and 0.9 hour in infants and children (n = 40).  
385 Area under the serum concentration time curves averaged 339 mcg•hr/mL in infants and children  
386 (n = 41), whereas the corresponding mean clavulanate area under the serum concentration time  
387 curves was approximately 7 mcg•hr/mL in the same population (n = 40).

388 Renal Impairment: An inverse relationship exists between the serum half-life of  
389 ticarcillin and creatinine clearance. The half-life of ticarcillin in patients with renal failure is  
390 approximately 13 hours. The dosage of TIMENTIN need only be adjusted in cases of severe  
391 renal impairment [*see Dosage and Administration (2.3)*].

392 Ticarcillin may be removed from patients undergoing dialysis; the actual amount  
393 removed depends on the duration and type of dialysis.

## 394 **12.4 Microbiology**

### 395 **Mechanism of action**

396 Ticarcillin disrupts bacterial cell wall development by inhibiting peptidoglycan synthesis  
397 and/or by interacting with penicillin-binding proteins.

398 Ticarcillin is susceptible to degradation by  $\beta$ -lactamases, so the spectrum of activity does  
399 not normally include organisms which produce these enzymes.

400 Clavulanic acid is a  $\beta$ -lactam, structurally related to the penicillins, which inactivates  
401 some  $\beta$ -lactamase enzymes commonly found in bacteria resistant to penicillins and  
402 cephalosporins. In particular, it has good activity against the clinically important  
403 plasmid-mediated  $\beta$ -lactamases frequently responsible for transferred drug resistance.

404 The formulation of ticarcillin with clavulanic acid in TIMENTIN protects ticarcillin from  
405 degradation by  $\beta$ -lactamase enzymes, effectively extending the antibacterial spectrum of  
406 ticarcillin to include many bacteria normally resistant to ticarcillin and other  $\beta$ -lactam  
407 antibacterials.

408

### 409 **Interaction with other antimicrobials**

410 *In vitro* synergism between TIMENTIN and gentamicin, tobramycin, or amikacin against  
411 multi-resistant isolates of *Pseudomonas aeruginosa* has been demonstrated.

412

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

415

416 **Gram-positive bacteria**  
417 *Staphylococcus aureus* (methicillin-susceptible isolates only)  
418 *Staphylococcus epidermidis* (methicillin-susceptible isolates only)

419  
420 **Gram-negative bacteria**

421 *Citrobacter* species  
422 *Enterobacter* species  
423 *E. cloacae*  
424 *Escherichia coli*  
425 *Haemophilus influenzae*<sup>a</sup>  
426 *Klebsiella* species  
427 *K. pneumoniae*  
428 *Pseudomonas* species  
429 *P. aeruginosa*  
430 *Serratia marcescens*

431  
432 **Anaerobic bacteria**

433 *Bacteroides fragilis* group  
434 *Prevotella melaninogenica*

435 <sup>a</sup>  $\beta$ -lactamase-negative, ampicillin-resistant (BLNAR) isolates of *H. influenzae* must be  
436 considered resistant to ticarcillin/clavulanic acid.

437  
438 The following in vitro data are available, but their clinical significance is unknown. At least 90  
439 percent of the following bacteria exhibit an *in vitro* minimum inhibitory concentration (MIC)  
440 less than or equal to the susceptible breakpoint for ticarcillin/clavulanic acid. However, the  
441 efficacy of ticarcillin/clavulanic acid in treating clinical infections due to these bacteria have not  
442 been established in adequate and well-controlled clinical trials.

443  
444 **Gram positive bacteria**

445 *Staphylococcus saprophyticus*  
446 *Streptococcus agalactiae* (Group B)  
447 *Streptococcus bovis*  
448 *Streptococcus pneumoniae* (penicillin-susceptible isolates only)  
449 *Streptococcus pyogenes*  
450 Viridans group streptococci

451

452 **Gram negative bacteria**

453 *Moraxella catarrhalis*

454 *Morganella morganii*

455 *Neisseria gonorrhoeae*

456 *Pasteurella multocida*

457 *Proteus mirabilis*

458 *Proteus penneri*

459 *Proteus vulgaris*

460 *Providencia rettgeri*

461 *Providencia stuartii*

462

463 **Anaerobic bacteria**

464 *Clostridium species*

465 *C. perfringens*

466 *C. difficile*

467 *C. sporogenes*

468 *C. ramosum*

469 *C. bifermentans*

470 *Eubacterium species*

471 *Fusobacterium species*

472 *F. nucleatum*

473 *F. necrophorum*

474 *Peptostreptococcus species*

475 *Veillonella species*

476

477 *Susceptibility Test Methods*

478 When available, the clinical microbiology laboratory should provide the results of in vitro  
479 susceptibility test results for antimicrobial drug products used in local hospitals and practice  
480 areas to the physician as periodic reports that describe the susceptibility profile of nosocomial  
481 and community-acquired pathogens. These reports should aid the physician in selecting an  
482 antibacterial drug product for treatment.

483

484 *Dilution Techniques*

485 Quantitative methods are used to determine antimicrobial MICs. These MICs provide estimates  
486 of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined  
487 using a standardized test method<sup>2,4</sup> (broth and/or agar). The MIC values should be interpreted  
488 according to criteria provided in Table 3.

489

490 *Diffusion Techniques*

491 Quantitative methods that require measurement of zone diameters can also provide reproducible  
 492 estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an  
 493 estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be  
 494 determined using a standardized test method.<sup>3,4</sup> These procedures use paper disks impregnated  
 495 with 85 mcg of ticarcillin/clavulanate potassium (75 mcg ticarcillin plus 10 mcg clavulanate  
 496 potassium) to test the susceptibility of bacteria to ticarcillin/clavulanic acid. The disc diffusion  
 497 interpretive criteria are provided in Table 3.

498  
 499 *Anaerobic Techniques*

500 For anaerobic bacteria, susceptibility to ticarcillin/clavulanic acid can be determined by  
 501 standardized test methods.<sup>4,5</sup> The MIC values obtained should be interpreted according to the  
 502 criteria in Table 3.

503  
 504

**Table 3. Susceptibility Test Interpretive Criteria for ticarcillin/clavulanic acid**

Microorganism	Minimum Inhibitory Concentration (mcg/mL)			Disc Diffusion Zone Diameter (mm)		
	S	I	R	S	I	R
Anaerobes	≤32/2	64/2	≥128/2	-	-	-
<i>Enterobacteriaceae</i>	≤16/2	32/2 - 64/2	≥128/2	≥20	15 - 19	≤14
<i>Pseudomonas aeruginosa</i>	≤16/2	32/2-64/2	≥128/2	≥24	16-23	≤15
<i>Staphylococci</i>	≤8/2	-	≥16/2	≥23	-	≤22

505  
 506 A report of “Susceptible” indicates the antimicrobial is likely to inhibit growth of the pathogen if  
 507 the antimicrobial compound reaches the concentrations at the infection site necessary to inhibit  
 508 growth of the pathogen. A report of “Intermediate” indicates that the result should be considered  
 509 equivocal, and, if the bacterium is not fully susceptible to alternative, clinically feasible drugs,  
 510 the test should be repeated. This category implies possible clinical applicability in body sites  
 511 where the drug product is physiologically concentrated or in situations where a high dosage of  
 512 the drug product can be used. This category also provides a buffer zone that prevents small  
 513 uncontrolled technical factors from causing major discrepancies in interpretation. A report of  
 514 “Resistant” indicates that the antimicrobial is not likely to inhibit growth of the pathogen if the  
 515 antimicrobial compound reaches the concentrations usually achievable at the infection site; other  
 516 therapy should be selected.

517  
 518 *Quality Control*

519 Standardized susceptibility test procedures require the use of laboratory controls to monitor and  
 520 ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques  
 521 of the individual performing the tests.<sup>2,3,4,5</sup> Standard ticarcillin/clavulanic acid powder should  
 522 provide the following range of MIC values noted in Table 4. For the diffusion technique using

523 the 85 mcg of ticarcillin/clavulanate potassium (75 mcg ticarcillin plus 10 mcg clavulanate  
524 potassium), the criteria in Table 4 should be achieved.

525

526 **Table 4. Acceptable Quality Control Ranges for Ticarcillin/Clavulanic Acid**

QC Strain	Broth MIC (mcg/mL)	Zone Diameter (mm)	Agar Dilution MIC (mcg/mL)
<i>Bacteroides thetaiotaomicron</i> ATCC 29741	0.5/2 – 2/2	-	0.5/2 – 2/2
<i>Escherichia coli</i> ATCC 25922	4/2 - 16/2	24 - 30	-
<i>Escherichia coli</i> ATCC 35218	8/2 - 32/2	21 - 25	-
<i>Eubacterium lentum</i> ATCC 43055	8/2 – 32/2	-	16/2 -64/2
<i>Pseudomonas aeruginosa</i> ATCC 27853	8/2 - 32/2	20 - 28	-
<i>Staphylococcus aureus</i> ATCC 29213	0.5/2 - 2/2	-	-
<i>Staphylococcus aureus</i> ATCC 25923	-	29 – 37	-

527 ATCC = American Type Culture Collection

528

## 529 **13 NONCLINICAL TOXICOLOGY**

### 530 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

531 Long-term studies in animals have not been performed to evaluate carcinogenic potential.  
532 Results from in vitro assays in bacteria (Ames tests), yeast, and human lymphocytes, and in vivo  
533 in mouse bone marrow (micronucleus test) indicate TIMENTIN is without genotoxic potential.

## 534 **14 CLINICAL STUDIES**

535 TIMENTIN has been studied in 296 pediatric patients (excluding neonates and infants  
536 less than 3 months) in 6 controlled clinical trials. The majority of patients studied had  
537 intra-abdominal infections, and the primary comparator was clindamycin and gentamicin with or  
538 without ampicillin. At the end-of-therapy visit, comparable efficacy was reported in the trial  
539 arms using TIMENTIN and an appropriate comparator.

540 TIMENTIN was also evaluated in an additional 408 pediatric patients (excluding  
541 neonates and infants less than 3 months) in 3 uncontrolled US clinical trials. Patients had a broad  
542 range of presenting diagnoses including: Infections in bone and joint, skin and skin structure,  
543 lower respiratory tract, urinary tract, as well as intra-abdominal and gynecologic infections.  
544 Patients received TIMENTIN, either 300 mg/kg/day (based on the ticarcillin component) divided  
545 every 4 hours for severe infection or 200 mg/kg/day (based on the ticarcillin component) divided  
546 every 6 hours for mild to moderate infections. Efficacy rates were comparable to those obtained  
547 in controlled trials.

548 The adverse event profile in these 704 pediatric patients treated with TIMENTIN was  
549 comparable to that seen in adult patients.

550 **15 REFERENCES**

- 551 1. Cockcroft, DW, et al. Prediction of Creatinine clearance from Serum Creatinine. *Nephron*  
552 16:31-41, 1976.
- 553 2. Clinical and Laboratory Standards Institute (CLSI). Methods for Dilution Antimicrobial  
554 Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard – 9<sup>th</sup> ed. CLSI  
555 Document M07-A9. CLSI, 950 West Valley Rd., Suite 2500, Wayne, PA 19087, 2012.
- 556 3. CLSI. Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved  
557 Standard – 11<sup>th</sup> ed. CLSI Document M02-A11. CLSI, 2012.
- 558 4. CLSI. Performance Standards for Antimicrobial Susceptibility Testing; 22<sup>nd</sup> Informational  
559 Supplement. CLSI document M100-S22. CLSI, 2012.
- 560 5. CLSI. Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved  
561 Standard – 8<sup>th</sup> ed. CLSI Document M11-A8. CLSI, 2012.

562 **16 HOW SUPPLIED/STORAGE AND HANDLING**

563 Each 3.1-gram vial of TIMENTIN for Injection contains sterile ticarcillin disodium  
564 equivalent to 3 grams ticarcillin and sterile clavulanate potassium equivalent to 0.1 gram  
565 clavulanic acid.

NDC 0029-6571-26            3.1-gram Vial

566 Each 31-gram Pharmacy Bulk Package of TIMENTIN for Injection contains sterile  
567 ticarcillin disodium equivalent to 30 grams ticarcillin and sterile clavulanate potassium  
568 equivalent to 1 gram clavulanic acid.

NDC 0029-6579-21            31-gram Pharmacy Bulk Package

569 Each 100-mL single-dose GALAXY (PL 2040) Plastic bag of TIMENTIN Injection in  
570 contains ticarcillin disodium equivalent to 3.0 grams ticarcillin and clavulanate potassium  
571 equivalent to 0.1 gram clavulanic acid.

NDC 0029-6571-31            100 mL GALAXY (PL 2040) Plastic Bag

572 3.1-gram Vials and 31-gram Pharmacy Bulk Packages of TIMENTIN for Injection  
573 should be stored at or below 24°C (75°F).

574 GALAXY (PL 2040) Plastic bags of TIMENTIN Injection should be stored at or below -  
575 20°C (-4°F). Avoid unnecessary handling of bags.

576 **Thawing of Plastic Bags:** Thaw frozen bag at room temperature 22°C (72°F) or in a  
577 refrigerator 4°C (39°F). [Do not force thaw by immersion in water baths or by microwave  
578 irradiation.] Check for minute leaks by squeezing bag firmly. If leaks are detected discard  
579 solution as sterility may be impaired. Do not add supplementary medication.

580 The bag should be visually inspected. Thawed solutions should not be used unless clear;  
581 solutions will be light to dark yellow in color. Components of the solution may precipitate in the  
582 frozen state and will dissolve upon reaching room temperature with little or no agitation. If, after  
583 visual inspection, the solution remains cloudy or if an insoluble precipitate is noted or if any  
584 seals or outlet ports are not intact, the bag should be discarded.

585           The thawed solution is stable for 24 hours at room temperature 22°C (72°F) or for 7 days  
586 under refrigeration 4°C (39°F).  
587           Do not refreeze.

## 588 **17    PATIENT COUNSELING INFORMATION**

### 589 **17.1   Information for Patients**

- 590   • Patients should be counseled that antibacterial drugs, including TIMENTIN, should only be  
591    used to treat bacterial infections. They do not treat viral infections (e.g., the common cold).  
592    When TIMENTIN is prescribed to treat a bacterial infection, patients should be told that  
593    although it is common to feel better early in the course of therapy, the medication should be  
594    taken exactly as directed. Skipping doses or not completing the full course of therapy may:  
595    (1) decrease the effectiveness of the immediate treatment, and (2) increase the likelihood that  
596    bacteria will develop resistance and will not be treatable by TIMENTIN or other antibacterial  
597    drugs in the future.
- 598   • Patients should be counseled that diarrhea is a common problem caused by antibacterials, and  
599    it usually ends when the antibacterial is discontinued. Sometimes after starting treatment with  
600    antibacterials, patients can develop watery and bloody stools (with or without stomach  
601    cramps and fever) even as late as 2 or more months after having taken their last dose of the  
602    antibacterial. If this occurs, patients should contact their physician as soon as possible.
- 603   • Patients should be aware that TIMENTIN contains a penicillin that can cause allergic  
604    reactions in some individuals.

605

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607 GALAXY is a registered trademark of Baxter International, Inc.

608



609

610 GlaxoSmithKline

611 Research Triangle Park, NC 27709

612

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