

## HIGHLIGHTS OF PRESCRIBING INFORMATION

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

### **VANCOCIN® (vancomycin hydrochloride, USP) CAPSULES** Initial U.S. Approval: 1986

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

#### -----RECENT MAJOR CHANGES-----

Dosage and Administration (12/2011)  
Warnings and Precautions (12/2011)

#### -----INDICATIONS AND USAGE-----

Treatment of: (1)

- *C. difficile*-associated diarrhea
- Enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains)

Important Limitations: (1) (5.1)

- Orally administered VANCOCIN is not effective for other types of infections.

#### -----DOSAGE AND ADMINISTRATION-----

- *C. difficile*-associated diarrhea:
  - Adult Patients (≥18 years of age): 125 mg orally 4 times daily for 10 days. (2.1)
  - Pediatric Patients (<18 years of age): 40 mg/kg in 3 or 4 divided doses for 7 to 10 days. The total daily dosage should not exceed 2 g. (2.2)
- Staphylococcal enterocolitis:
  - Adult Patients (≥18 years of age): 500 mg to 2 g orally in 3 or 4 divided doses for 7 to 10 days. (2.1)
  - Pediatric Patients (<18 years of age): 40 mg/kg in 3 or 4 divided doses for 7 to 10 days. The total daily dosage should not exceed 2 g. (2.2)

#### -----DOSAGE FORMS AND STRENGTHS-----

- 125 mg capsules (3)
- 250 mg capsules (3)

#### -----CONTRAINDICATIONS-----

Hypersensitivity to vancomycin (4)

#### -----WARNINGS/PRECAUTIONS-----

- VANCOCIN must be given orally for treatment of staphylococcal enterocolitis and *C. difficile*-associated diarrhea. Orally administered VANCOCIN CAPSULES are not effective for other types of infections. (5.1)
- Clinically significant serum concentrations have been reported in some patients who have taken multiple oral doses of VANCOCIN for active *C. difficile*-associated diarrhea. Monitoring of serum concentrations may be appropriate in some instances. (5.2)
- Nephrotoxicity has occurred following oral VANCOCIN therapy and can occur either during or after completion of therapy. The risk is increased in geriatric patients (5.3) Monitor renal function.
- Ototoxicity has occurred in patients receiving VANCOCIN. (5.4) Assessment of auditory function may be appropriate in some instances.
- Prescribing VANCOCIN in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria. (5.6)

#### -----ADVERSE REACTIONS-----

The most common adverse reactions (≥ 10%) were nausea (17%), abdominal pain (15%), and hypokalemia (13%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact ViroPharma at (888-651-0201) or FDA at 1-800-FDA-1088 ([www.fda.gov/medwatch](http://www.fda.gov/medwatch)).

#### -----DRUG INTERACTIONS-----

No drug interaction studies have been conducted. (7)

#### -----USE IN SPECIFIC POPULATIONS-----

- **Pediatrics:** Safety and effectiveness in patients <18 years of age have not been established. (8.4)
- **Geriatrics:** In patients >65 years of age, including those with normal renal function prior to treatment, renal function should be monitored during and following treatment with VANCOCIN to detect potential vancomycin induced nephrotoxicity. (5.3) (6.1) (8.5) (14.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: December 2011

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\*Sections or subsections omitted from the Full Prescribing Information are not listed.

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## 2 FULL PRESCRIBING INFORMATION

### 3 VANCOCIN<sup>®</sup> (vancomycin hydrochloride, USP) CAPSULES

#### 4 1 INDICATIONS AND USAGE

5 VANCOCIN CAPSULES are indicated for the treatment of *C. difficile*-associated  
6 diarrhea. VANCOCIN CAPSULES are also used for the treatment of enterocolitis  
7 caused by *Staphylococcus aureus* (including methicillin-resistant strains). Parenteral  
8 administration of vancomycin is not effective for the above infections; therefore,  
9 VANCOCIN CAPSULES must be given orally for these infections.

#### 10 **Orally administered VANCOCIN is not effective for other types of infections.**

11 To reduce the development of drug-resistant bacteria and maintain the effectiveness of  
12 VANCOCIN CAPSULES and other antibacterial drugs, VANCOCIN CAPSULES  
13 should be used only to treat infections that are proven or strongly suspected to be caused  
14 by susceptible bacteria. When culture and susceptibility information are available, they  
15 should be considered in selecting or modifying antibacterial therapy. In the absence of  
16 such data, local epidemiology and susceptibility patterns may contribute to the empiric  
17 selection of therapy.

#### 18 2 DOSAGE AND ADMINISTRATION

##### 19 2.1 Adults

20 VANCOCIN CAPSULES are used in treating *C. difficile*-associated diarrhea and  
21 staphylococcal enterocolitis.

- 22 • *C. difficile*-associated diarrhea: The recommended dose is 125 mg administered  
23 orally 4 times daily for 10 days.
- 24 • Staphylococcal enterocolitis: Total daily dosage is 500 mg to 2 g administered  
25 orally in 3 or 4 divided doses for 7 to 10 days.

##### 26 2.2 Pediatric Patients

27 The usual daily dosage is 40 mg/kg in 3 or 4 divided doses for 7 to 10 days. The total  
28 daily dosage should not exceed 2 g.

#### 29 3 DOSAGE FORMS AND STRENGTHS

30 VANCOCIN 125 mg\* CAPSULES have an opaque blue cap and opaque brown body  
31 imprinted with “3125” on the cap and “VANCOCIN HCL 125 MG” on the body in white  
32 ink.

33 VANCOCIN 250 mg\* CAPSULES have an opaque blue cap and opaque lavender body  
34 imprinted with “3126” on the cap and “VANCOCIN HCL 250 MG” on the body in white  
35 ink.

36 \*Equivalent to vancomycin.

## 37 **4 CONTRAINDICATIONS**

38 VANCOCIN CAPSULES are contraindicated in patients with known hypersensitivity to  
39 vancomycin.

## 40 **5 WARNINGS AND PRECAUTIONS**

### 41 **5.1 Oral Use Only**

42 **This preparation for the treatment of colitis is for oral use only and is not**  
43 **systemically absorbed. VANCOCIN CAPSULES must be given orally for treatment**  
44 **of staphylococcal enterocolitis and *Clostridium difficile*-associated diarrhea. Orally**  
45 **administered VANCOCIN CAPSULES are not effective for other types of**  
46 **infections.**

47 **Parenteral administration of vancomycin is *not* effective for treatment of**  
48 **staphylococcal enterocolitis and *C. difficile*-associated diarrhea. If parenteral**  
49 **vancomycin therapy is desired, use an intravenous preparation of vancomycin and**  
50 **consult the package insert accompanying that preparation.**

### 51 **5.2 Potential for Systemic Absorption**

52 Clinically significant serum concentrations have been reported in some patients who have  
53 taken multiple oral doses of VANCOCIN for active *C. difficile*-associated diarrhea. Some  
54 patients with inflammatory disorders of the intestinal mucosa also may have significant  
55 systemic absorption of vancomycin. These patients may be at risk for the development of  
56 adverse reactions associated with higher doses of VANCOCIN; therefore, monitoring of  
57 serum concentrations of vancomycin may be appropriate in some instances, e.g., in  
58 patients with renal insufficiency and/or colitis or in those receiving concomitant therapy  
59 with an aminoglycoside antibiotic.

### 60 **5.3 Nephrotoxicity**

61 Nephrotoxicity (e.g., reports of renal failure, renal impairment, blood creatinine  
62 increased) has occurred following oral VANCOCIN therapy in randomized controlled  
63 clinical studies, and can occur either during or after completion of therapy.

64 The risk of nephrotoxicity is increased in patients >65 years of age (*see ADVERSE*  
65 *REACTIONS, Clinical Trial Experience [6.1] and USE IN SPECIFIC POPULATIONS,*  
66 *Geriatric Use [8.5]*).

67 In patients >65 years of age, including those with normal renal function prior to  
68 treatment, renal function should be monitored during and following treatment with  
69 VANCOCIN to detect potential vancomycin induced nephrotoxicity.

#### 70 **5.4 Ototoxicity**

71 Ototoxicity has occurred in patients receiving vancomycin. It may be transient or  
72 permanent. It has been reported mostly in patients who have been given excessive  
73 intravenous doses, who have an underlying hearing loss, or who are receiving  
74 concomitant therapy with another ototoxic agent, such as an aminoglycoside. Serial tests  
75 of auditory function may be helpful in order to minimize the risk of ototoxicity (*see*  
76 *ADVERSE REACTIONS, Postmarketing Experience [6.2]*).

#### 77 **5.5 Superinfection**

78 Use of VANCOCIN may result in the overgrowth of nonsusceptible bacteria. If  
79 superinfection occurs during therapy, appropriate measures should be taken.

#### 80 **5.6 Development of Drug-Resistant Bacteria**

81 Prescribing VANCOCIN in the absence of a proven or strongly suspected bacterial  
82 infection is unlikely to provide benefit to the patient and increases the risk of the  
83 development of drug resistant bacteria.

### 84 **6 ADVERSE REACTIONS**

#### 85 **6.1 Clinical Trial Experience**

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

89 The data described below reflect exposure to VANCOCIN in 260 adult subjects in two  
90 Phase 3 clinical trials for the treatment of diarrhea associated with *C. difficile*. In both  
91 trials, subjects received VANCOCIN 125 mg orally four times daily. The mean duration  
92 of treatment was 9.4 days. The median age of patients was 67, ranging between 19 and 96  
93 years of age. Patients were predominantly Caucasian (93%) and 52% were male.

94 Adverse reactions occurring in  $\geq 5\%$  of VANCOCIN-treated subjects are shown in Table  
 95 1. The most common adverse reactions associated with VANCOCIN ( $\geq 10\%$ ) were  
 96 nausea, abdominal pain, and hypokalemia.

97 **Table 1: Common ( $\geq 5\%$ ) Adverse Reactions<sup>a</sup> for VANCOCIN Reported in Clinical Trials for**  
 98 **Treatment of Diarrhea Associated with *C. difficile***

System/Organ Class	Adverse Reaction	VANCOCIN % (N=260)
<b>Gastrointestinal disorders</b>	Nausea	17
	Abdominal pain	15
	Vomiting	9
	Diarrhea	9
	Flatulence	8
<b>General disorders and administration site conditions</b>	Pyrexia	9
	Edema peripheral	6
	Fatigue	5
<b>Infections and infestations</b>	Urinary tract infection	8
<b>Metabolism and nutrition disorders</b>	Hypokalemia	13
<b>Musculoskeletal and connective tissue disorders</b>	Back pain	6
<b>Nervous system disorders</b>	Headache	7
<sup>a</sup> Adverse reaction rates were derived from the incidence of treatment-emergent adverse events.		

99 Nephrotoxicity (e.g., reports of renal failure, renal impairment, blood creatinine  
 100 increased) occurred in 5% of subjects treated with VANCOCIN. Nephrotoxicity  
 101 following VANCOCIN typically first occurred within one week after completion of  
 102 treatment (median day of onset was Day 16). Nephrotoxicity following VANCOCIN  
 103 occurred in 6% of subjects  $>65$  years of age and 3% of subjects  $\leq 65$  years of age (*see*  
 104 *WARNINGS AND PRECAUTIONS, Nephrotoxicity [5.3]*).

105 The incidences of hypokalemia, urinary tract infection, peripheral edema, insomnia,  
 106 constipation, anemia, depression, vomiting, and hypotension were higher among subjects  
 107  $>65$  years of age than in subjects  $\leq 65$  years of age (*see USE IN SPECIFIC*  
 108 *POPULATIONS, Geriatric Use [8.5]*).

109 Discontinuation of study drug due to adverse events occurred in 7% of subjects treated  
 110 with VANCOCIN. The most common adverse events leading to discontinuation of  
 111 VANCOCIN were *C. difficile* colitis ( $<1\%$ ), nausea ( $<1\%$ ), and vomiting ( $<1\%$ ).

## 112 **6.2 Postmarketing Experience**

113 The following adverse reactions have been identified during post-approval use of  
114 VANCOCIN. Because these reactions are reported voluntarily from a population of  
115 uncertain size, it is not always possible to reliably estimate their frequency or establish a  
116 causal relationship to drug exposure.

117 *Ototoxicity:* Cases of hearing loss associated with intravenously administered  
118 vancomycin have been reported. Most of these patients had kidney dysfunction or a  
119 preexisting hearing loss or were receiving concomitant treatment with an ototoxic drug  
120 (see *WARNINGS AND PRECAUTIONS, Ototoxicity [5.4]*). Vertigo, dizziness, and  
121 tinnitus have been reported.

122 *Hematopoietic:* Reversible neutropenia, usually starting 1 week or more after onset of  
123 intravenous therapy with vancomycin or after a total dose of more than 25 g, has been  
124 reported for several dozen patients. Neutropenia appears to be promptly reversible when  
125 vancomycin is discontinued. Thrombocytopenia has been reported.

126 *Miscellaneous:* Patients have been reported to have had anaphylaxis, drug fever, chills,  
127 nausea, eosinophilia, rashes (including exfoliative dermatitis), Stevens-Johnson  
128 syndrome, toxic epidermal necrolysis, and rare cases of vasculitis in association with the  
129 administration of vancomycin.

130 A condition has been reported that is similar to the IV-induced syndrome with symptoms  
131 consistent with anaphylactoid reactions, including hypotension, wheezing, dyspnea,  
132 urticaria, pruritus, flushing of the upper body (“Red Man Syndrome”), pain and muscle  
133 spasm of the chest and back. These reactions usually resolve within 20 minutes but may  
134 persist for several hours.

## 135 **7 DRUG INTERACTIONS**

136 No drug interaction studies have been conducted.

## 137 **8 USE IN SPECIFIC POPULATIONS**

### 138 **8.1 Pregnancy**

139 Pregnancy Category B – The highest doses of vancomycin tested were not teratogenic in  
140 rats given up to 200 mg/kg/day IV (1180 mg/m<sup>2</sup> or 1 times the recommended maximum  
141 human dose based on body surface area) or in rabbits given up to 120 mg/kg/day IV  
142 (1320 mg/m<sup>2</sup> or 1.1 times the recommended maximum human dose based body surface  
143 area). No effects on fetal weight or development were seen in rats at the highest dose

144 tested or in rabbits given 80 mg/kg/day (880 mg/m<sup>2</sup> or 0.74 times the recommended  
145 maximum human dose based on body surface area).

146 In a controlled clinical study, the potential ototoxic and nephrotoxic effects of  
147 vancomycin on infants were evaluated when the drug was administered intravenously to  
148 pregnant women for serious staphylococcal infections complicating intravenous drug  
149 abuse. Vancomycin was found in cord blood. No sensorineural hearing loss or  
150 nephrotoxicity attributable to vancomycin was noted. One infant whose mother received  
151 vancomycin in the third trimester experienced conductive hearing loss that was not  
152 attributed to the administration of vancomycin. Because the number of subjects treated in  
153 this study was limited and vancomycin was administered only in the second and third  
154 trimesters, it is not known whether vancomycin causes fetal harm. Because animal  
155 reproduction studies are not always predictive of human response, VANCOCIN should  
156 be given to a pregnant woman only if clearly needed.

### 157 **8.3 Nursing Mothers**

158 Vancomycin is excreted in human milk based on information obtained with the  
159 intravenous administration of vancomycin. However, systemic absorption of  
160 vancomycin is very low following oral administration of VANCOCIN (*see CLINICAL*  
161 *PHARMACOLOGY, Pharmacokinetics [12.3]*). It is not known whether vancomycin is  
162 excreted in human milk, as no studies of vancomycin concentration in human milk after  
163 oral administration have been done. Caution should be exercised when VANCOCIN is  
164 administered to a nursing woman. Because of the potential for adverse events, a decision  
165 should be made whether to discontinue nursing or discontinue the drug, taking into  
166 account the importance of the drug to the mother.

### 167 **8.4 Pediatric Use**

168 Safety and effectiveness in pediatric patients have not been established.

### 169 **8.5 Geriatric Use**

170 In clinical trials, 54% of VANCOCIN-treated subjects were >65 years of age. Of these,  
171 40% were between the ages of >65 and 75, and 60% were >75 years of age.

172 Clinical studies with VANCOCIN in diarrhea associated with *Clostridium difficile* have  
173 demonstrated that geriatric subjects are at increased risk of developing nephrotoxicity  
174 following treatment with oral VANCOCIN, which may occur during or after completion  
175 of therapy. In patients >65 years of age, including those with normal renal function prior  
176 to treatment, renal function should be monitored during and following treatment with  
177 VANCOCIN to detect potential vancomycin induced nephrotoxicity (*see WARNINGS*

178 *AND PRECAUTIONS, Nephrotoxicity [5.3]; ADVERSE REACTIONS, Clinical Trial*  
179 *Experience [6.1] and CLINICAL STUDIES, Diarrhea Associated with Clostridium*  
180 *difficile [14.1]).*

181

182 Patients >65 years of age may take longer to respond to therapy compared to patients ≤65  
183 years of age (*see CLINICAL STUDIES, Diarrhea Associated with Clostridium difficile*  
184 *[14.1]).* Clinicians should be aware of the importance of appropriate duration of  
185 VANCOCIN treatment in patients >65 years of age and not discontinue or switch to  
186 alternative treatment prematurely.

187

## 188 **10 OVERDOSAGE**

189 Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is  
190 poorly removed by dialysis. Hemofiltration and hemoperfusion with polysulfone resin  
191 have been reported to result in increased vancomycin clearance.

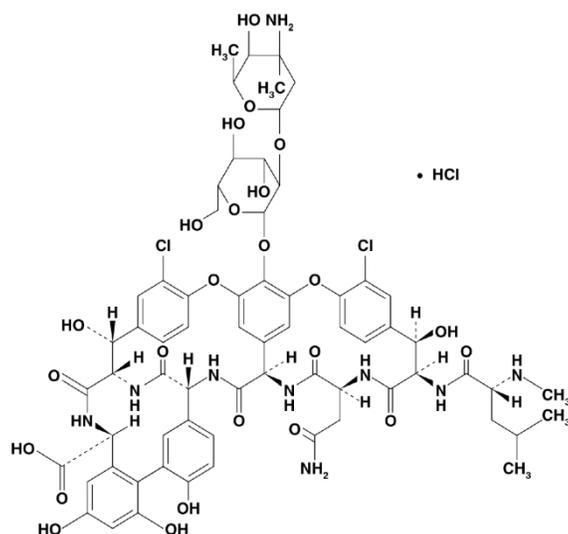
192 To obtain up-to-date information about the treatment of overdose, a good resource is your  
193 certified Regional Poison Control Center. Telephone numbers of certified poison control  
194 centers are listed in the *Physicians' Desk Reference (PDR)*. In managing overdose,  
195 consider the possibility of multiple drug overdoses, interaction among drugs, and unusual  
196 drug kinetics.

## 197 **11 DESCRIPTION**

198 VANCOCIN CAPSULES for oral administration contain chromatographically purified  
199 vancomycin hydrochloride, a tricyclic glycopeptide antibiotic derived from  
200 *Amycolatopsis orientalis* (formerly *Nocardia orientalis*), which has the chemical formula  
201  $C_{66}H_{75}Cl_2N_9O_{24} \cdot HCl$ . The molecular weight of vancomycin hydrochloride is 1485.73;  
202 500 mg of the base is equivalent to 0.34 mmol.

203 The capsules contain vancomycin hydrochloride equivalent to 125 mg (0.08 mmol) or  
204 250 mg (0.17 mmol) vancomycin. The capsules also contain F D & C Blue No. 2,  
205 gelatin, iron oxide, polyethylene glycol, titanium dioxide, and other inactive ingredients.

206 Vancomycin hydrochloride has the structural formula:



207

## 208 12 CLINICAL PHARMACOLOGY

### 209 12.1 Mechanism of Action

210 Vancomycin is an antibacterial drug (*see CLINICAL PHARMACOLOGY, Microbiology*  
211 *[12.4]*).

### 212 12.3 Pharmacokinetics

213 Vancomycin is poorly absorbed after oral administration. During multiple dosing of 250  
214 mg every 8 hours for 7 doses, fecal concentrations of vancomycin in volunteers exceeded  
215 100 mg/kg in the majority of samples. No blood concentrations were detected and  
216 urinary recovery did not exceed 0.76%. In anephric subjects with no inflammatory bowel  
217 disease who received vancomycin oral solution 2 g for 16 days, blood concentrations of  
218 vancomycin were less than or equal to 0.66  $\mu\text{g/mL}$  in 2 of 5 subjects. No measurable  
219 blood concentrations were attained in the other 3 subjects. Following doses of 2 g daily,  
220 concentrations of drug were  $>3100$  mg/kg in the feces and  $<1$   $\mu\text{g/mL}$  in the serum of  
221 subjects with normal renal function who had *C. difficile*-associated diarrhea. After  
222 multiple-dose oral administration of vancomycin, measurable serum concentrations may  
223 occur in patients with active *C. difficile*-associated diarrhea, and, in the presence of renal  
224 impairment, the possibility of accumulation exists. It should be noted that the total  
225 systemic and renal clearances of vancomycin are reduced in the elderly (*see USE IN*  
226 *SPECIFIC POPULATIONS, Geriatric Use [8.5]*).

227 **12.4 Microbiology**

228 Mechanism of action

229 The bactericidal action of vancomycin against *Staphylococcus aureus* and the vegetative  
230 cells of *Clostridium difficile* results primarily from inhibition of cell-wall biosynthesis.  
231 In addition, vancomycin alters bacterial-cell-membrane permeability and RNA synthesis.

232 Mechanism of resistance

233 *Staphylococcus aureus*

234 *S. aureus* isolates with vancomycin minimal inhibitory concentrations (MICs) as  
235 high as 1024 mcg/mL have been reported.

236 The exact mechanism of this resistance is not clear but is believed to be due to  
237 cell wall thickening and potentially the transfer of genetic material.

238 *Clostridium difficile*

239 Isolates of *C. difficile* generally have vancomycin MICs of <1 mcg/mL, however  
240 vancomycin MICs ranging from 4 mcg/mL to 16 mcg/mL have been reported.

241 The mechanism which mediates *C. difficile*'s decreased susceptibility to  
242 vancomycin has not been fully elucidated.

243 Vancomycin has been shown to be active against susceptible isolates of the following  
244 bacteria in clinical infections as described in the INDICATIONS AND USAGE section.

245 Gram-positive bacteria

246 *Staphylococcus aureus* (including methicillin-resistant isolates) associated with  
247 enterocolitis

248 Anaerobic Gram-positive bacteria

249 *Clostridium difficile* isolates associated with *C. difficile* associated diarrhea.

250 **13 NONCLINICAL TOXICOLOGY**

251 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

252 No long-term carcinogenesis studies in animals have been conducted.

253 At concentrations up to 1000 µg/mL, vancomycin had no mutagenic effect *in vitro* in the  
254 mouse lymphoma forward mutation assay or the primary rat hepatocyte unscheduled  
255 DNA synthesis assay. The concentrations tested *in vitro* were above the peak plasma  
256 vancomycin concentrations of 20 to 40 µg/mL usually achieved in humans after slow  
257 infusion of the maximum recommended dose of 1 g. Vancomycin had no mutagenic

258 effect *in vivo* in the Chinese hamster sister chromatid exchange assay (400 mg/kg IP) or  
259 the mouse micronucleus assay (800 mg/kg IP).

260 No definitive fertility studies have been conducted.

## 261 **14 CLINICAL STUDIES**

### 262 **14.1 Diarrhea Associated with *Clostridium difficile***

263 In two trials, VANCOCIN 125 mg orally four times daily for 10 days was evaluated in  
264 266 adult subjects with *C. difficile*-associated diarrhea (CDAD). Enrolled subjects were  
265 18 years of age or older and received no more than 48 hours of treatment with oral  
266 VANCOCIN or oral/intravenous metronidazole in the 5 days preceding enrollment.  
267 CDAD was defined as  $\geq 3$  loose or watery bowel movements within the 24 hours  
268 preceding enrollment, and the presence of either *C. difficile* toxin A or B, or  
269 pseudomembranes on endoscopy within the 72 hours preceding enrollment. Subjects with  
270 fulminant *C. difficile* disease, sepsis with hypotension, ileus, peritoneal signs or severe  
271 hepatic disease were excluded.

272

273 Efficacy analyses were performed on the Full Analysis Set (FAS), which included  
274 randomized subjects who received at least one dose of VANCOCIN and had any post-  
275 dosing investigator evaluation data (N=259; 134 in Trial 1 and 125 in Trial 2).

276

277 The demographic profile and baseline CDAD characteristics of enrolled subjects were  
278 similar in the two trials. VANCOCIN-treated subjects had a median age of 67 years, were  
279 mainly white (93%), and male (52%). CDAD was classified as severe (defined as 10 or  
280 more unformed bowel movements per day or  $WBC \geq 15000/mm^3$ ) in 25% of subjects, and  
281 47% were previously treated for CDAD.

282

283 Efficacy was assessed by using clinical success, defined as diarrhea resolution and the  
284 absence of severe abdominal discomfort due to CDAD, on Day 10. An additional  
285 efficacy endpoint was the time to resolution of diarrhea, defined as the beginning of  
286 diarrhea resolution that was sustained through the end of the prescribed active treatment  
287 period.

288

289 The results for clinical success for VANCOCIN-treated subjects in both trials are shown  
290 in Table 2.

291

292 **Table 2: Clinical Success Rates (Full Analysis Set)**

	<b>Clinical Success Rate</b>	<b>95% Confidence Interval</b>
	<b>VANCOCIN % (N)</b>	
<b>Trial 1</b>	81.3 (134)	(74.4, 88.3)
<b>Trial 2</b>	80.8 (125)	(73.5, 88.1)

293  
 294 The median time to resolution of diarrhea was 5 days and 4 days in Trial 1 and Trial 2,  
 295 respectively. For subjects older than 65 years of age, the median time to resolution was 6  
 296 days and 4 days in Trial 1 and Trial 2, respectively. In subjects with diarrhea resolution  
 297 at end-of-treatment with VANCOCIN, recurrence of CDAD during the following four  
 298 weeks occurred in 25 of 107 (23%) and 18 of 102 (18%) in Trial 1 and Trial 2,  
 299 respectively.

300

301 Restriction Endonuclease Analysis (REA) was used to identify *C. difficile* baseline  
 302 isolates in the BI group. In Trial 1, the Vancocin-treated subjects were classified at  
 303 baseline as follows 31 (23%) with BI strain, 69 (52%) with non-BI strain, and 34 (25%)  
 304 with unknown strain. Clinical success rates were 87% for BI strain, 81% for non-BI  
 305 strain, and 76% for unknown strain. In subjects with diarrhea resolution at end-of  
 306 treatment with VANCOCIN, recurrence of CDAD during the following four weeks  
 307 occurred in 7 of 26 subjects with BI strain, 12 of 56 subjects with non-BI strain, and 6 of  
 308 25 subjects with unknown strain.

309

## 310 **16 HOW SUPPLIED/STORAGE AND HANDLING**

311 VANCOCIN CAPSULES are available in:

312

313 The 125 mg\* capsules have an opaque blue cap and opaque brown body imprinted with  
 314 “3125” on the cap and “VANCOCIN HCL 125 MG” on the body in white ink. A carton  
 315 contains 2 blister packs. Each blister pack contains 10 capsules for a total of 20 capsules  
 316 per carton. NDC 66593-3125-2 (PU3125)

317

318 The 250 mg\* capsules have an opaque blue cap and opaque lavender body imprinted with  
 319 “3126” on the cap and “VANCOCIN HCL 250 MG” on the body in white ink. A carton  
 320 contains 2 blister packs. Each blister pack contains 10 capsules for a total of 20 capsules  
 321 per carton. NDC 66593-3126-2 (PU3126)

322

323 Store at controlled room temperature, 59° to 86°F (15° to 30°C).

324

325 \*Equivalent to vancomycin.

326

327 **17 PATIENT COUNSELING INFORMATION**

328 Patients should be counseled that antibacterial drugs including VANCOCIN should only  
329 be used to treat bacterial infections. They do not treat viral infections (e.g., the common  
330 cold). When VANCOCIN is prescribed to treat a bacterial infection, patients should be  
331 told that although it is common to feel better early in the course of therapy, the  
332 medication should be taken exactly as directed. Skipping doses or not completing the full  
333 course of therapy may (1) decrease the effectiveness of the immediate treatment and (2)  
334 increase the likelihood that bacteria will develop resistance and will not be treatable by  
335 VANCOCIN or other antibacterial drugs in the future.

336

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337 VANCOCIN<sup>®</sup> is a registered U.S. trademark owned by ViroPharma Incorporated.

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