REVIEW ARTICLE e-ISSN: 2349-0659 p-ISSN; 2350-0964

A Review on Tigecycline: Its Usage, Mechanism of Action, and Clinical Efficacy

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Abstract

Tigecycline is the first drug in the glycylcycline antimicrobial structurally related to minocycline. This antibiotic marketed by Wyeth Pharmaceuticals under the brand name Tygacil. Tigecycline has a broad spectrum of activity against drug-resistant Gram-positive, Gram-negative, aerobic, and atypical bacterial species including bacterial isolates resistant to beta-lactams and fluoroquinolones. Tigecycline is concentrated in cells and is eliminated primarily via biliary excretion. Diminished renal function does not significantly alter its systemic clearance. Trials of tigecycline have shown its efficacy for the treatment of complicated skin and skin structure infections, complicated intra-abdominal infections, and community-acquired bacterial pneumonia in adults. 50 mg intravenous dose of tigecycline at every 12 hours showed adverse conditions like nausea, vomiting and diarrhoea that may lead discontinuation of tigecycline use in therapy. The overuse of antibiotics in humans as well as in animals has given rise to a condition which is known as antibiotic resistance.

Keywords: Clinical efficacy, Generic brands, Pharmacokinetics, Resistance mechanism, Risk factors, Tigecycline

Asian Pac. J. Health Sci., (2026); DOI: 10.21276/apjhs.2026.13.2.07

Introduction

Tetracyclines are broad-spectrum antibiotics that have been in use since the mid-1900s, but recently, their use has been limited due to alterations in efflux pumps and ribosomal protection proteins which cause resistance to these agents. Glycylcyclines were developed to overcome these resistance mechanisms. Alterations to the tetracycline structures allowed tigecycline to maintain activity against tetracycline-resistant organisms, penicillin-susceptible and resistant *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus* and *Staphylococcus epidermadis*, glycopeptide-intermediate *S. aureus*, and vancomycin-resistant *Enterococcus* spp. At present, tigecycline (previously GAR-936) is the only antibiotic of this class in clinical use. Food and Drug Administration (FDA) on June 15, 2005[1] approved tigecycline as the first antibiotic in the glycylcycline class.

In 2008, a small pathogen group was reported as "the ESKAPE bugs: *Enterococcus faecium*, *S. aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species.[2] These pathogens currently cause the majority of worldwide hospital infections and effectively "escape" the effects of antibacterial drugs. Tigecycline is a most useful therapeutic agent for polymicrobial infections, especially in cases which required deep tissue penetration or also in multidrug-resistant (MDR) pathogens suspected cases.[3] Tigecycline is active *in vitro* against a variety of Gram-positive and Gram-negative organisms, including nosocomial resistant pathogens such as vancomycin-resistant enterococci (VRE), Methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, and multidrug-resistant (MDR) *Acinetobacter* spp.[4]

The new era of antibiotics, tigecycline, is an established second-generation tetracycline-class antibacterial agent developed for the treatment of polymicrobial MDR pathogens, including Gram-positive and Gram-negative organisms. FDA issued an alert that tigecycline significantly increased the risk of mortality in the management of patients with severe infections; however, with the rise of drug resistance among Enterobacteriaceae through the production of several beta-lactamases, tigecycline becomes a potential option given its ability to evade common mechanisms of acquired tetracycline resistance. In addition, FDA has given the early warnings about high mortality rates, especially when given as monotherapy; combination therapy with tigecycline seems essential.[5]

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How to cite this article: Singh A, Ahsan S. A Review on Tigecycline: Its Usage, Mechanism of Action, and Clinical Efficacy. Asian Pac. J. Health Sci., 2026;13(2):43-51.

Source of support: Nil.

Conflicts of interest: None.

Received: 18/05/2026 **Revised:** 29/05/2026 **Accepted:** 19/06/2026

Description of Tigecycline

Marketed as TYGACIL (tigecycline) 50 mg powder for injection.

Chemical Structure of Tigecycline

The chemical name of tigecycline is (4S,4aS,5aR,12aS)-9-[2-(tert-butylamino)acetamido]-4,7bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2naphthacenecarboxamide [Figure 1]. The empirical formula is $C_{29}H_{39}N_5O_8$ and the molecular weight is 585.65. CAS Registry Number is 220620-09-7.

Tigecycline is an orange lyophilized powder or cake. The reconstitution solution is yellow to orange, essentially free of particulate matter. Each TYGACIL vial contains 50 mg tigecycline

lyophilized powder for intravenous infusion. Each vial contains 100 mg of lactose. The pH is adjusted with hydrochloric acid, and if necessary, with sodium hydroxide.[5]

Tigecycline metabolism

Tigecycline is not extensively metabolized. In 2007, it was reported that the primary route of tigecycline elimination (unaltered) is biliary excretion (59%), while secondary routes of elimination include renal excretion (22% unchanged through urine) and glucuronidation.[6] *In vitro* studies with tigecycline using human liver microsomes, liver slices, and hepatocytes led to the formation of only trace amounts of metabolites. In healthy males, ^{14}C-labeled tigecycline was recovered in urine and feces, but a glucuronide, an N-acetyl metabolite, and a tigecycline epimer (≥10) were also present. Mass balance and excretion studies with ^{14}C-labeled tigecycline in rats and dogs revealed ~50% fecal elimination of tigecycline and 35% excretion through urine as unchanged drug. Studies in humans also revealed the major route of tigecycline elimination through feces (59%), while 32% through urine.[7] Based on *in vitro* studies, it was found that for critically ill patients and those on multiple therapeutic agents, tigecycline does not affect the cytochrome P450 (CYP450) enzyme family (CYP1A2, CYP2C8, CYP2C19, CYP2D6, and CYP3A4), and also does not alter the metabolism of drugs metabolized by CYP450 enzymes.[8]

The pharmacokinetics of tigecycline are not affected by food, although tolerability is increased if the drug is administered following a meal.[7] The pharmacokinetic profile of tigecycline is not affected by severe or end-stage renal disease, and also, tigecycline is not eliminated by hemodialysis.[9] These factors make dosing of tigecycline straightforward and uncomplicated. *In vitro* protein binding in human plasma is concentration-dependent and ranges from 71% at 0.1 mg/L to 87% at 10 mg/L. Tigecycline distribution and concentration in human tissue versus serum are shown in Table 1.

Mechanism of Action

Tigecycline enters bacterial cells through energy-dependent pathways or with passive diffusion and inhibits protein translation in bacteria by binding to the 30S subunit of the ribosome. It acts by blocking the entry of aminoacyl transfer ribonucleic acid molecules into the A site of the ribosome to inhibit protein synthesis.[11,12] This prevents incorporation of amino acid residues into elongating peptide chains. Tigecycline carries a glycylamido moiety attached to the 9-position of minocycline. The substitution pattern is not present in any naturally occurring or semisynthetic tetracycline and imparts certain microbiologic properties to tigecycline. Tigecycline is not affected by major tetracycline resistance mechanisms of ribosomal protection and is not affected by many efflux systems. Tigecycline is an antibiotic for systemic use with broad-spectrum activity against aerobic and facultative Gram-positive and Gram-negative bacteria and anaerobic bacteria.[13] Tigecycline is active *in vitro* against antibiotic-resistant bacteria such as VRE (*Enterococcus faecalis* and *E. faecium*), MRSA, ESBL-producing Gram-negative bacteria, and carbapenem-resistant bacteria.[14,15]

Spectrum of Activity

Tigecycline has been approved for complicated skin and soft tissue infections and complicated intra-abdominal infections (cIAIs).[16] It shows activity against a variety of aerobic Gram-positive and Gram-negative pathogens in comparison with other tetracyclines [Table 2]. In clinical skin and skin structure infections, tigecycline exhibits *in vivo* activity against methicillin-susceptible *S. aureus*, MRSA, *Streptococcus agalactiae, Streptococcus anginosus* group (*S. anginosus, S. intermedius*, and *S. constellatus*), *Streptococcus pyogenes*, vancomycin-susceptible *E. faecalis*, *Escherichia coli*, and *Bacteroides fragilis. In vivo* trials of intra-abdominal infections also exhibit activity against the following organisms: Vancomycin-susceptible *E. faecalis*, methicillin-susceptible *S. aureus*, *S. anginosus*, *Citrobacter freundii*, *Enterobacter cloacae*, *E. coli*, *Klebsiella oxytoca*, *K. pneumoniae*, *B. fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Clostridium perfringens*, and *Peptostreptococcus micros.*[17]

In vitro activity has also been defined in a variety of other organisms such as *Enterococcus avium*, *E. faecium*, *Enterococcus casseliflavus*, and *E. faecalis* (vancomycin-susceptible and -resistant isolates), *Listeria monocytogenes, Staphylococcus epidermis* (vancomycin susceptible and resistant), *Staphylococcus haemolyticus, A. baumannii*, *Aeromonas hydrophila*, *Citrobacter*

Table 1: Distribution of tigecycline in tissue versus serum[8,10]

Tissue/Fluid	*Concentration in tissue versus serum*	*AUC_{0-12} ratio tissue: Serum*	*AUC_{0-24} ratio site: Serum*
Gallbladder*	38-fold	-	23/14
Lung*	8.6-fold	-	2.0/2.0
Colon*	2.3-fold	-	2.6/1.8
Bone*	0.35- fold	-	0.41/0.28
Bile*	-	-	537/368
Synovial fluid*	0.58-fold	-	0.31/0.32
CSF*	-	-	0.11/0.12
Skin blister fluid#	26% lower than serum	1.6/2.18	-
Alveolar macrophages#	78-fold	134/1.73	-
Epithelial lining fluid#	32% greater than serum	2.28/1.73	-

*Patients received a single 100 mg intravenous dose of tigecycline before surgery, #Healthy subjects received a single 100 mg intravenous dose of tigecycline followed by 50 mg intravenously every 12 h

Table 2: Acceptable quality control ranges for susceptibility testing of tigecycline source[5]

Quality control organism	*Minimum inhibitory concentrations (mcg/mL)*	*Disk diffusion (Zone diameters in mm)*
Staphylococcus aureus ATCC 25923	NA	20–25
S. aureus ATCC 29213	0.03–0.25	NA
Escherichia coli ATCC 25922	0.03–0.25	20–27
Enterococcus faecalis ATCC 29212	0.03–0.12	NA
Streptococcus pneumoniae ATCC 49619	0.016–0.12	23–29
Haemophilus influenzae ATCC 49247	0.06–0.5	23–31
Bacteroides fragilis ATCC 25285 (Agar dilution)	0.12–1	NA
Bacteroides thetaiotaomicron ATCC 29741(Agar dilution)	0.5–2	NA
Eubacterium lentum ATCC 43055 (Agar dilution)	0.06–0.5	NA
Clostridium difficile ATCC 70057 (Agar dilution)	0.12–1	NA

ATCC: American type culture collection, NA: Not applicable

koseri, *Enterobacter aerogenes*, *Pasteurella multocida*, *Serratia marcescens*, and *Stenotrophomonas maltophilia*. Activity against a variety of anaerobes and mycobacteria has also been observed.[17]

Tigecycline is more active against MRSA and *Staphylococcus epidermidis* than susceptible strains of these organisms. Tigecycline has established improved activity against penicillin-susceptible, penicillin-intermediate, and penicillin-resistant strains of *S. pneumoniae* and against *Enterococcus* species when compared with tetracyclines. Tigecycline has better activity against *L. monocytogenes* than tetracycline. Tigecycline activity is improved *in vitro* when compared with the other tetracyclines against the following organisms: *C. freundii*, *E. coli*, *Enterobacter cloacae*, *Klebsiella* species, *Salmonella* species, *S. marcescens*, and *Shigella* species. Tigecycline and minocycline cover *Acinetobacter* species.[18] According to a recent study, polymyxin B and colistin were observed as very good drugs for the treatment of metallo-beta-lactamase-producing *A. baumannii* with 0.8% and 0% resistance rates in comparison of tigecycline with 6% resistance rate. However, due to the toxicity of polymyxins, tigecycline is the next better drug of choice with 94% susceptibility rates.[19] Tigecycline is also less active than minocycline against *Burkholderia cepacia* and *S. maltophilia*. According to some studies, tigecycline is not active against *P. aeruginosa*, *Proteus* species, *Morganella,* and *Providencia* species.[4,20-22]

Quality Control Organisms' Susceptibility Ranges for Tigecycline

As with other susceptibility techniques, the use of laboratory control microorganisms is required to control the technical aspects of the laboratory standardized procedures.[23-26] Minimum inhibitory concentration values were determined using standard tigecycline powder and the diffusion technique using the 15 mcg tigecycline disk provided in Table 2.

Tigecycline Usage in Clinical Practice

After the introduction of tigecycline in clinical practice, it was intended as a new weapon for empiric and targeted treatment against difficult-to-treat infections. Tigecycline was initially approved by the United States FDA in 2005 and the European Medicines Agency in 2006 for the treatment of cIAI and complicated skin and skin structure infections (cSSSI) and other indications.[27] In 2008, FDA also approved it for the treatment of community-acquired bacterial pneumonia (CABP).[28] Tygacil is not approved by the FDA for treatment of diabetic foot infection, hospital-acquired pneumonia, and ventilator-associated pneumonia.[5] Studies have shown that the combination of tigecycline with imipenem and cilastatin sodium is effective for treating acute pancreatitis complicated by abdominal infections. This combination therapy can rapidly relieve clinical symptoms, improve clinical outcomes, and demonstrate a favorable safety profile.[29]

Clinical efficacy of tigecycline

cIAIs

In 2003, the Infectious Diseases Society of America published updated guidelines for the treatment of cIAI and recommended ampicillin/sulbactam, cefazolin-metronidazole, or ertapenem to treat mild to moderate cIAI. For oral therapy, a fluoroquinolone (e.g., levofloxacin) plus metronidazole or amoxicillin/clavulanate alone is recommended for treatment. Treatment of high-risk patients (severe or postoperative nosocomial IAI) is recommended with carbapenems (e.g., imipenem/cilastatin, ertapenem, or meropenem), piperacillin/tazobactam, fluoroquinolone plus metronidazole, or a third- or fourth-generation cephalosporin (e.g., ceftriaxone, cefepime) plus metronidazole. Infections that extend beyond a hollow viscous within the abdomen to produce peritonitis or abscess are known as Intra-abdominal infections.[30]

In 2005, A pooled analysis of two phase III, multicentre, double blind, randomized trials (301 and 306 studies) was done to compare clinical efficacy and safety of tigecycline monotherapy vs imipenem cilastatin in 1642 patients with cIAIs. Pooled analysis findings reported clinically evaluable population cure rates of 86.7% for tigecycline versus 87.1% for imipenem-cilastatin. This pooled analysis reported *in vitro* activity of tigecycline against typically resistant organisms (e.g., ESBL-producing *E. coli* and *Klebsiella* species, MRSA, VRE). This suggested tigecycline as an effective and well-tolerated monotherapy option for treatment of patients with cIAI.[31]

cSSSI

In 2005, the Infectious Diseases Society of America guidelines recommend nafcillin or cefazolin for patients with cSSSI caused by suspected methicillin-sensitive *S. aureus*. Patients allergic to penicillin can be treated with clindamycin or vancomycin. cSSSI caused by suspected MRSA can be treated with vancomycin or linezolid. A combination of penicillin/beta-lactamase inhibitor, e.g., ampicillin/sulbactam or piperacillin/tazobactam, or combination of fluroquinolone/clindamycin can be used for treatment of cSSSI caused by multiple organisms.[32]

Findings of this pooled analysis indicated that tigecycline monotherapy is efficacious and statistically non-inferior to the combination of vancomycin-aztreonam across several categories of patient populations at the test-of-cure (TOC) visit. No significant differences in clinical cure rates were observed between the two treated groups with tigecycline and vancomycin-aztreonam in the microbiologically evaluable population. Efficacy of tigecycline against many isolates (*S. aureus, S. pyogenes, E. coli, E. faecalis, S. agalactiae,* and *B. fragilis*) commonly linked to cSSSI was demonstrated in this pooled analysis. The eradication rate of MRSA was 78.1% in the tigecycline group versus 76% in the vancomycin-aztreonam group. MIC_{90} values of tigecycline were consistently low (0.25 mg/L) for both methicillin-resistant and methicillin-susceptible *S. aureus*.

A significantly higher number of tigecycline-treated patients ($P \leq 0.032$) reported treatment-emergent adverse events related to the digestive tract (anorexia, diarrhea, nausea, vomiting, and dyspepsia) in comparison with vancomycin-aztreonam-treated patients ($P < 0.001$). The number of patients in the modified intent-to-treat (mITT) population who discontinued therapy because of adverse events was greater in the vancomycin-aztreonam-treated group than in the tigecycline group ($P = 0.188$). This pooled analysis concluded that tigecycline monotherapy is as safe and efficacious as vancomycin-aztreonam for the treatment of cSSSI.

CABP

The pooled analysis revealed the findings of two phase III, multicenter, randomized, double blind studies (308 and 313) to

compare clinical efficacy and safety of tigecycline monotherapy (100 mg intravenous initial dose followed by 50 mg every 12 h) versus levofloxacin (500 mg intravenous every 12 or 24 h) in patients with cIAIs.[26] Study 308 was conducted in the United States, Canada, and Latin America, and study 313 included Europe, Asia Pacific, and South Africa. The total therapy period was 7–14 days. The primary efficacy endpoints at the TOC visit in the clinically evaluable and clinical mITT (c-mITT) patient populations are given in Table 3.

In two crucial studies, clinical cure rates by infecting pathogens in both types of microbiologically evaluable patients treated with tigecycline and levofloxacin showed following findings: clinical cure rates in *Haemophilus influenzae* causing infections were 82.4% with tigecycline and 81.3% with levofloxacin; in *Legionella pneumophila* causing infections were 100% with each of the drug tigecycline or levofloxacin; whereas clinical cure rates in infections caused by *S. pneumoniae* (penicillin-susceptible) were reported as 95.7% with tigecycline and 88.6% with levofloxacin. These studies again show the clinical efficacy of tigecycline monotherapy.

Table 3: Clinical cure rates from two pivotal studies in community-acquired bacterial pneumonia (Source: Wyeth Pharmaceuticals;[17] Reference ID 3379756)

Studies	*Tigecycline n/N (%)*	*Levofloxacin n/N (%)*	*95% confidence interval (CI)*
Study 308*			
CE	125/138 (90.6)	136/156 (87.2)	(−4.4, 11.2)
c-mITT	149/191 (78)	158/203 (77.8)	(−8.5, 8.9)
Study 313			
CE	128/144 (88.9)	116/136 (85.3)	(−5.0, 12.2)
c-mITT	170/203 (83.7)	163/200 (81.5)	(−5.6, 10.1)

*After 3 days of intravenous therapy, a switch to oral levofloxacin (500 mg daily) was permitted for both treatment populations in study 308

Mechanism of resistance

Tigecycline is not affected by most of the common antibiotic resistance mechanisms used by bacteria to abolish antibiotic therapy, due to hindrance generated by the large D-ring substituent.[4] Tigecycline resistance in some bacteria (e.g., *Acinetobacter calcoaceticus-A. baumannii* complex) is associated with MDR efflux pumps.

Chemical Structure of Tigecycline Prevail Over Resistance

Bacteria use one or more of four principal mechanisms to resist antimicrobial agents [Figure 2].[11,33]

- The antimicrobial agents are inactivated through enzymatic degradation, e.g., in beta-lactamase-producing bacteria
- The target penicillin-binding proteins are structurally altered to prevent antibiotic binding to the targets, e.g., in the unmodified tetracyclines
- Changes in cell wall permeability that stop entry of the antibiotic into the cell interior, e.g., with fluoroquinolones and β-lactams
- Antibiotics are excluded from the cell by efflux pumps, e.g., with fluoroquinolones and β-lactams.

Tetracycline resistance has emerged in an increasing number of bacterial species over decades of use, and efflux is the leading tetracycline resistance mechanism as observed in *E. coli*.[34] The most common resistance mechanisms to this class of antibiotics result from the acquisition of genetically mobile tetracycline resistance (tet) genes, which encode efflux pump proteins that eject tetracyclines from the cell (e.g., tet A-E, tet G-L) or code for proteins that protect the ribosomes (e.g., tet M, tet O).[35,36] Figure 3 illustrates modifications in the four-ring carbocyclic skeleton of tetracyclines. The addition of a modified glycylamido moiety to the D ring overcame both efflux and ribosomal type resistance. Tigecycline (C29H39N5O8, MW 585.65 Da) was formed by the addition of a side chain (9-tert-butyl-glycylamido moiety) at the 9th position of D ring of minocycline. This derivative was found to possess expanded microbiological and therapeutic benefits.[4,37,38] This attached group facilitates the molecule to bind to the ribosome up to 5 times more tightly which in turn decreases the probability of resistance development. Due to the presence of this large D-ring substituent, tigecycline is not affected by most of the common antibiotic resistance mechanisms.[4] Tigecycline binds to the 30S ribosomal subunit and inhibits protein synthesis even in the presence of ribosomal protection mechanisms. This antibiotic is also excluded from efflux pumps.[38] Other antibiotic resistance mechanisms (target site modifications, enzymatic degradation of antimicrobial agents, and DNA gyrase mutations) affect other antimicrobial agents but do not affect tigecycline or other glycylcyclines. It is observed in *E. coli* that overproduction of the AcrAB multidrug efflux pump leads to decrease tigecycline susceptibility.[34]

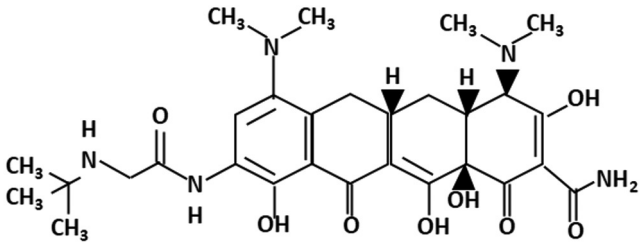

Figure 1: Chemical structure of tigecycline

Mechanism of Tigecycline Resistance in Different Pathogens

The most common mechanism of resistance to tigecycline from literature was reported as overexpression of different efflux pumps in both naturally susceptible isolates and also in the naturally resistant species [Table 4].

However, recently, the development of adjuvant therapies and novel antimicrobials is crucial. Several compounds are currently under preclinical evaluation, aiming to restore tigecycline efficacy by targeting resistance mechanisms like efflux pumps.[60] Chemical compounds that inhibit the function, expression, and assembly of efflux pumps are being developed.[61] Previously, susceptibility to TIG was restored by 1-(1-naphthylmethyl)-piperazine through upregulation of the AcrAB efflux pump.[62] Lysine has demonstrated a synergistic effect against the tmexCD-toprJ efflux pump in *K. pneumoniae*, *E. coli*, *S. aureus,* and *E. faecalis*.[63] Resistance nodulation division inhibitors have also been reported; ML-7 hydrochloride potentiates TIG activity in *K. pneumoniae*.[64]

Drug interactions of Tygacil[17,65]

In a drug interaction study, tigecycline (100 mg dose, followed by 50 mg intravenously every 12 h) and digoxin (0.5 mg dose

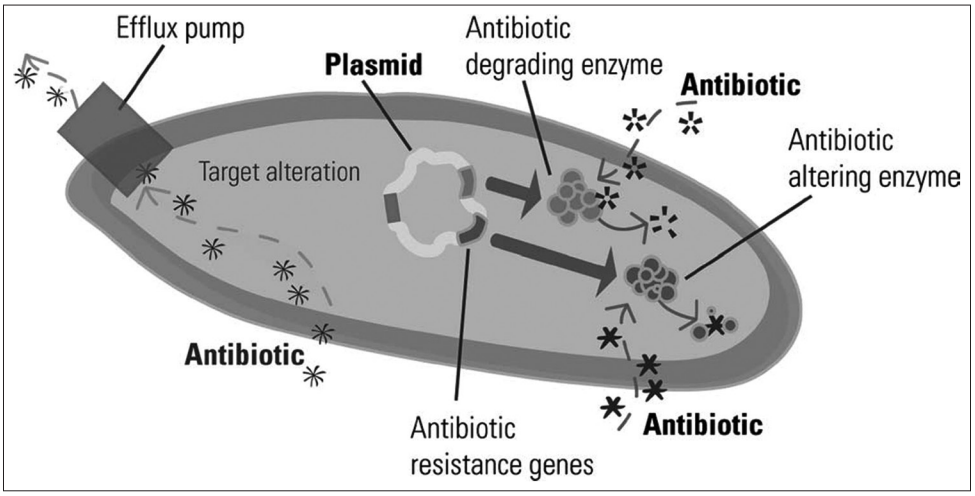

Figure 2: Target molecules are structurally altered to avoid antibiotic binding; antibiotics are excluded from cell entry; they are inactivated through enzymatic degradation, for example; or they are pumped out of the cell (efflux). Source: Andersson[33]

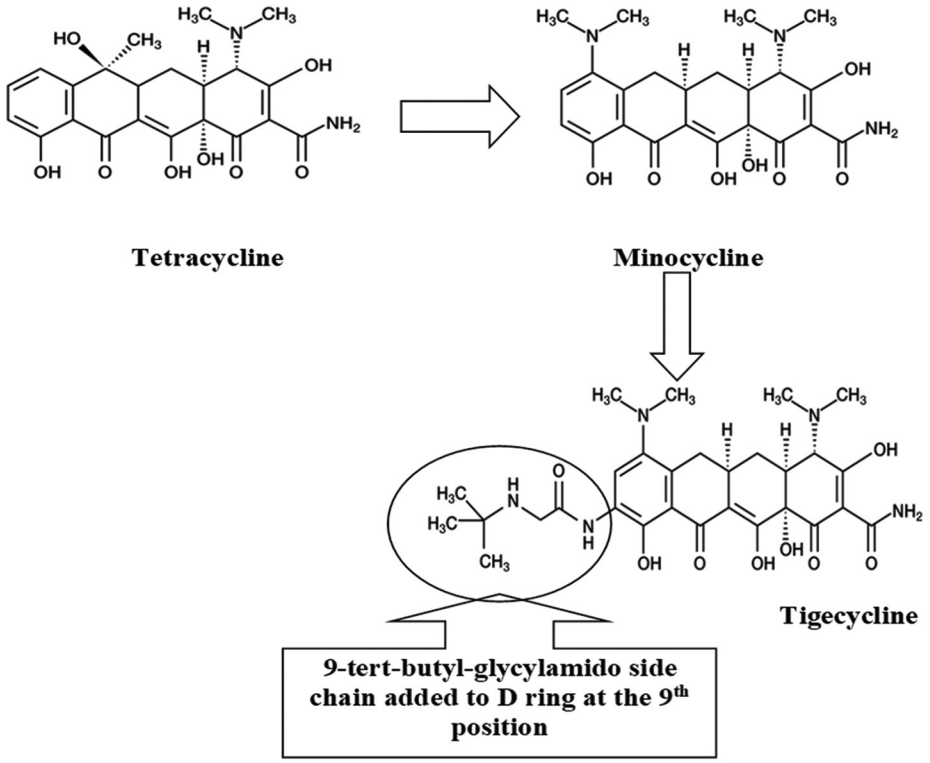

Figure 3: Chemical structures of tetracycline, minocycline, and tigecycline[11]

followed by 0.25 mg, orally every 24 h) were coadministered to healthy subjects. As a result, tigecycline slightly decreased the maximum concentration of drug (C_{max}) of digoxin by 13% but did not affect the area under the concentration-time curve (area under the curve [AUC]) or clearance of digoxin. The small change in C_{max} did not affect the steady-state pharmacodynamic effects of digoxin. Digoxin also did not affect the pharmacokinetic profile of tigecycline. Therefore, Tygacil can be administered with digoxin.[66] Tygacil does not alter the metabolism of drugs metabolized by the following 6 CYP450 isoforms (1A2, 2C8, 2C9, 2C19, 2D6, and 3A4), while these drugs are not expected to alter the clearance of tigecycline.[17]

Another study of concomitant administration of Tygacil (100 mg followed by 50 mg every 12 h) and warfarin (25 mg single-dose) to healthy subjects showed a decrease in clearance of R-warfarin and S-warfarin by 40% and 23%, respectively. Concurrent use of antibiotics with oral contraceptives may render oral contraceptives less effective. Based on an *in vitro* study, tigecycline is a P-glycoprotein (P-gp) substrate. Co-administration of P-gp inhibitors (e.g., ketoconazole or cyclosporine) or P-gp

Table 4: Reports on possible mechanisms of tigecycline resistance in various pathogens

Pathogen name	*Possible mechanism of resistance*	*References*
Pseudomonas aeruginosa	MexXY-OprM efflux pump-mediated resistance to tigecycline	[39]
Proteus mirabilis	AcrAB transport system appears to be associated with the intrinsic reduced susceptibility to tigecycline	[40]
Escherichia coli	Tigecycline is a possible substrate of resistance nodulation cell division (RND) -type multicomponent efflux transporters (AcrAB and AcrEF)	[41]
Klebsiella pneumoniae	RamA decreases tigecycline susceptibility owing to its role in expression of the AcrAB multidrug efflux pump	[42]
Bacteroides fragilis	TetX protein modifies tigacycline to form 11a-hydroxytigecycline, this modified molecule shows a weakened ability to inhibit protein translation in comparison to tigecycline.	[43]
Methicillin-resistant *Staphylococcus aureus*	Decreased susceptibility to tigecycline due to overexpression of mepA, a novel MATE family efflux pump	[44]
Enterobacter cloacae	RamA-mediated overexpression of the AcrAB efflux pump resulted in decreased susceptibility to tigecycline	[45]
Acinetobacter baumannii	Efflux mediated by the RND-type transporter AdeABC reduced tigecycline susceptibility	[46]
E. coli	A frameshift mutation due to loss of MarR functionality resulted in constitutive overproduction of MarA and AcrAB and decreased susceptibility to tigecycline	[47]
Klebsiella pneumoniae	High-level resistance to tigecycline resulted due to overexpression of regulatory genes, soxS and ramA.	[48]
Burkholderia cepacia complex	Efflux pump proteins have evolved tigecycline resistance but the use of inhibitors can restore the activity of tigecycline.	[49]
Salmonella enterica	Combination of two resistance mechanisms, Tn1721-tet(A) and inactivation of ramA gene results in resistance to tigecycline	[50]
Enterobacter cloacae	Exposure to ciprofloxacin selected for AcrAB upregulation resulted in tigecycline cross resistance	[51]
K. pneumoniae	Deletions, insertions, and point mutations in ramR gene may lead to reduce tigecycline sensitivity	[52]
A. baumannii	Overexpression of the AdeABC efflux pump resulted in tigecycline resistance	[53]
Acinetobacter calcoaceticus-A. baumannii complex	Overexpression of the AdeABC efflux pump is a prevalent mechanism to decrease tigecycline susceptibility	[54]
Serratia marcescens	Upregulation of endogenous SdeXY-HasF-mediated efflux pump resulted in tigecycline resistance	[55]
S. enterica	AcrAB and AcrEF confer tigecycline resistance. Overexpression of ramA and inactivation of RamR also increase tigecycline resistance in an AcrAB-dependent manner	[56]
K. pneumoniae	Overexpression of ramA and upregulation of acrA gene reduce tigecycline resistance	[57]
B. fragilis	Presence of text and tetX1 genes in *Bacteroids* strains exhibiting elevated MICs for tigecycline and might be a possible reason for tigecycline resistance	[58]
Bacteroides thetaiotaomicron	The flavin-dependent monooxygenase TetX confers resistance to all tetracyclines including tigecycline	[59]

MIC: Minimum inhibitory concentration

inducers (e.g., rifampicin) could affect the pharmacokinetics of tigecycline.[65,67]

Effect of Alkaloid (ALK) on Tigecycline Activity

Human serum albumin (HSA) has a very significant role in the transport of drugs. A study was conducted to investigate the effect of ALK (caffeine [CAF]) and flavonoids (FLAVs) (catechin, quercetin, and diosmin) on the binding of tigecycline (TGC) to HSA using multiple spectroscopic measurements and docking simulations.[68] Spectroscopic analyses of this study revealed that triple complexes of HSA-TGC-CAF/FLAVs are formed without problems and have higher binding affinities than double HSA-TGC. In addition, tigecycline does not change the microenvironments around the tryptophan and tyrosine residues in the presence of ALK and FLAVs.

Preclinical Safety Data

Repeated-dose toxicity studies in rats and dogs showed lymphoid depletion/atrophy of lymph nodes, spleen, and thymus, leukocytes, decreased erythrocytes, reticulocytes, and platelets, in association with bone marrow hypocellularity, and adverse renal and gastrointestinal effects with tigecycline (at exposures of 8 and 10 times the human daily dose based on AUC in rats and dogs, respectively). These alterations were found to be reversible after 2 weeks of dosing. Bone discoloring was observed in rats and was not found to be reversible after 2 weeks of dosing.

Results of some animal studies illustrate that tigecycline crosses the placenta and is found in fetal tissues. Decreased fetal weights in rats and rabbits (with associated delays in ossification) and fetal loss in rabbits have been observed with tigecycline in reproductive toxicity studies. Tigecycline was not teratogenic in the rat or rabbit. Tigecycline did not affect mating or fertility in rats at exposures up to 4.7 times the human daily dose based on AUC. In female rats, there were no compound-related effects on ovaries or estrus cycles at exposures up to 4.7 times the human daily dose based on AUC.

Some animal studies using ^{14}C-labeled tigecycline indicated excretion of tigecycline via the milk of lactating rats. Studies to evaluate the carcinogenic potential of tigecycline have not been performed, but short-term genotoxicity studies of

tigecycline were negative. Bolus intravenous administration of tigecycline has been associated with a histamine response in animal studies. These effects were observed at exposures of 14 and 3 times the human daily dose based on the AUC in rats and dogs, respectively.

No evidence of photosensitivity was observed in rats following administration of tigecycline.[65,67]

Tigecycline Manufacturer And Brand Names

Medindia regularly update their database as new generics are approved and become available in pharmacies. According to their data, the generic tigecycline is currently manufactured by six companies. The information provided includes quantity and the type of drug (Medindia[67] Last Updated on July 10, 2023; assessed on May 12, 2026). Medindia's database currently has 6 brands of generic tigecycline listed below [Table 5].

Table 5: Brand names of tigecycline

S. No.	*Brand name*	*Manufacturers*	*Type*	*Unit*
1.	Protigi (50 mg)	Progen Nutraceuticals Pvt. Ltd.	Injection	50 mg/vial
2.	Tigaphar (50 mg)	Zyphars Pharmaceuticals Pvt. Ltd	Injection	50 mg/vial
3.	Tygacil	Pfizer Ltd.	Injection	50 mg/vial
4.	Tigez (50 mg)	Lupin Laboratories Ltd.	Injection	50 mg/vial
5.	Tize (50 mg)	Health Biotech Pvt. Ltd.	Injection	50 mg/vial
6.	Trectabin (50 mg)	RSM Kilitch Pharma Pvt. Ltd.	Injection	50 mg/vial

Storage and handling of tigecycline[17]

Wyeth Tygacil (tigecycline) injection is supplied in a single-dose 5 mL glass vial or 10 mL glass vial, each vial containing 50 mg tigecycline lyophilized powder for reconstitution. Tygacil is supplied as: 5 mL- 10 vials/box. (NDC 0008-4990-02), 10 mL- 10 vials/box. (NDC 0008-4990-20).

Before reconstitution, Tygacil should be stored at 20–25°C. Transportation of Tygacil is permitted at 15–30°C. Reconstituted Tygacil can be stored at 25°C for up to 24 h and up to 6 h in the vial. If the storage conditions exceed 25°C after reconstitution, tigecycline should be used immediately. Alternatively, Tygacil mixed with 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP may be stored refrigerated at 2–8°C for up to 48 h following immediate transfer of the reconstituted solution into the intravenous bag or must be transferred and further diluted for intravenous infusion.

Patient Counseling Information Regarding Tygacil Use

Patients should be advised to use Tygacil (tigecycline) only to treat bacterial infections not to treat viral infections (e.g., the common cold). When Tygacil is prescribed to treat a bacterial infection, medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may decrease the effectiveness of the immediate treatment and increase the likelihood that bacteria will develop resistance and will not be treatable by Tygacil or other antibacterial drugs in the future. The common problem caused by antibiotics is diarrhea, which usually ends when the antibiotic is discontinued. Sometimes, at the start of treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) or even as late as 2 or more months after having the last dose of the antibiotic. If this occurs, patients urgently need to contact their physician.[17] In 2025, a study of 25 patients who received tigecycline as an anti-infective agent showed a treatment efficacy rate of 96%, appropriate utilization in 96% of cases, and an adverse event rate of 4%.[69]

Conclusion

Tigecycline (TIG) exhibits broad-spectrum antimicrobial activity against a wide range of Gram-negative and Gram-positive bacteria, including multidrug-resistant pathogens. Although its clinical use is frequently associated with gastrointestinal adverse effects, particularly nausea and vomiting, the observed increase in mortality has been attributed to reduced therapeutic efficacy in certain clinical settings rather than to direct drug toxicity. Mutations in the tet gene are a big problem to generate resistance pattern of tigecycline. More studies are required to overcome the problem of tigecycline. However, tigecycline (TIG) is considered one of the last-line therapeutic options for the treatment of MDR and extensively drug-resistant (XDR) bacterial infections. To preserve its clinical effectiveness and minimize the emergence of resistance, its use should be restricted to microbiologically confirmed MDR/XDR infections. In parallel, the implementation of active genomic surveillance for tet(X) variants, together with the adoption of a One Health approach, is essential for monitoring the emergence and transboundary dissemination of tigecycline resistance. These coordinated strategies are critical for limiting the spread of resistance determinants and safeguarding the long-term efficacy of tigecycline.

Authors Contributions

Anuradha Singh: Conceptualization, Resources, Data Curation, Writing-Original Draft, Writing-Reviewing and Editing, Saima Ahsan: Review and editing.

Ethical approval

Not required.

References

1. FDA Approves Tygacil; 2005. Available from: https://www.drugs.com/newdrugs/tygacil-wyeth-pharmaceuticals-complicated-skin-intra-abdominal-infections-101.html [Last accessed on 2025 Sep].
2. Rice LB. Federal funding for the study of antimicrobial resistance in nosocomial pathogens: No ESKAPE. J Infect Dis 2008;197:1079-81.
3. Stein GE, Craig WA. Tigecycline: A critical analysis. Clin Infect Dis 2006;43:518-24.
4. Pankey GA. Tigecycline. J Antimicrob Chemother 2005;56:470-80.
5. US Food and Drug Administration. FDA Drug Safety Podcast: FDA Warns of Increased Risk of Death with IV Antibacterial Tygacil (Tigecycline) and Approves New Boxed Warning. Silver Spring, MD: US Food and Drug Administration; 2013. Available from: http://www.fda.gov/drugs/drugsafety/drugsafetypodcasts/ucm370626.htm [Last accessed on 2015 Sep 26].
6. Hoffmann M, DeMaio W, Jordan RA, Talaat R, Harper D, Speth J, *et al*. Metabolism, excretion, and pharmacokinetics of [14C]tigecycline, a first-in-class glycylcycline antibiotic, after intravenous infusion to healthy male subjects. Drug Metab Dispos 2007;35:1543-53.

7. Meagher AK, Ambrose PG, Grasela TH, Ellis-Grosse EJ. The pharmacokinetic and pharmacodynamic profile of tigecycline. Clin Infect Dis 2005;41 Suppl 5:S333-40.
8. Peterson LR. A review of tigecycline--the first glycylcycline. Int J Antimicrob Agents 2008;32 Suppl 4:S215-22.
9. MacGowan AP. Tigecycline pharmacokinetic/pharmacodynamic update get access arrow. J Antimicrob Chemother 2008;62:i11-6.
10. Rodvold KA, Gotfried MH, Cwik M, Korth-Bradley JM, Dukart G, Ellis-Grosse EJ. Serum, tissue and body fluid concentrations of tigecycline after a single 100 mg dose. J Antimicrob Chemother 2006;58:1221-9.
11. Petersen PJ, Jacobus NV, Weiss WJ, Sum PE, Testa RT. *In vitro* and *in vivo* antibacterial activities of a novel glycylcycline, the 9-t-butylglycylamido derivative of minocycline (GAR-936). Antimicrob Agents Chemother 1999;43:738-44.
12. Bauer G, Berens C, Projan SJ, Hillen W. Comparison of tetracycline and tigecycline binding to ribosomes mapped by dimethylsulphate and drug-directed Fe2+ cleavage of 16S rRNA. J Antimicrob Chemother 2004;53:592-9.
13. Nicolau DP. Management of complicated infections in the era of antimicrobial resistance: The role of tigecycline. Expert Opin Pharmacother 2009;10:1213-22.
14. Kresken M, Leitner E, Brauers J, Geiss HK, Halle E, Von Eiff C, *et al*. Susceptibility of common aerobic pathogens to tigecycline: Results of a surveillance study in Germany. Eur J Clin Microbiol Infect Dis 2009;28:83-90.
15. Kresken M, Leitner E, Seifert H, Peters G, Von Eiff C. Susceptibility of clinical isolates of frequently encountered bacterial species to tigecycline one year after the introduction of this new class of antibiotics: Results of the second multicentre surveillance trial in Germany (G-TEST II, 2007). Eur J Clin Microbiol Infect Dis 2009;28:1007-11.
16. European Medicines Agency. Tygacil (Tigecycline): EPAR-Summary of Product Characteristics. Amsterdam: European Medicines Agency; 2014. Available from: https://www.ema.europa.eu/ema [Last accessed on 2015 Sep 15].
17. Wyeth Pharmaceuticals. Tygacil Prescribing Information; 2013. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021821s026s031lbl.pdf [Last accessed on 2026 Jan].
18. Pachón-Ibáñez ME, Jiménez-Mejías ME, Pichardo C, Llanos AC, Pachón J. Activity of tigecycline (GAR-936) against *Acinetobacter baumannii* strains, including those resistant to imipenem. Antimicrob Agents Chemother 2004;48:4479-81.
19. Sarada V, Rao R, Mani R, Ramana KV. Colistin, polymyxin B and tigecycline susceptibility to metallo betalactamase producing *Acinetobacter baumannii* isolated from tertiary health care hospital. Am J Microbiol Res 2014;2:60-2.
20. Bradford PA, Weaver-Sands DT, Petersen PJ. *In vitro* activity of tigecycline against isolates from patients enrolled in phase 3 clinical trials of treatment for complicated skin and skin-structure infections and complicated intra-abdominal infections. Clin Infect Dis 2005;41 Suppl 5:S315-32.
21. Greer ND. Tigecycline (tygacil): The first in the glycylcycline class of antibiotics. Proc (Bayl Univ Med Cent) 2006;19:155-61.
22. Bhattacharya M, Parakh A, Narang M. Tigecycline. J Postgrad Med 2009;55:65-8.
23. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. 9th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
24. Clinical and Laboratory Standards Institute. Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria. 8th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
25. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests. 11th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
26. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. 23rd Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.
27. Guo B, Li P, Qin B, Wang S, Zhang W, Shi Y, *et al*. An analysis of differences in carbapenem-resistant enterobacterales in different regions: A multicenter cross-sectional study. BMC Infect Dis 2024;24:116.
28. Tanaseanu C, Bergallo C, Teglia O, Jasovich A, Oliva ME, Dukart G, *et al*. Integrated results of 2 phase 3 studies comparing tigecycline and levofloxacin in community-acquired pneumonia. Diagn Microbiol Infect Dis 2008;61:329-38.
29. Zhu D, Hui Y, Lyu P. Efficacy of tigecycline combined with imipenem and cilastatin sodium in the treatment of SAP complicated with abdominal infection and its effect on serum AMS, ghrelin and LPS. J Med Syst 2023;8:5-8.
30. Solomkin JS, Mazuski JE, Baron EJ, Sawyer RG, Nathens AB, DiPiro JT, *et al*. Guidelines for the selection of anti-infective agents for complicated intra-abdominal infections. Clin Infect Dis 2003;37:997-1005.
31. Babinchak T, Ellis-Grosse E, Dartois N, Rose GM, Loh E, Tigecycline 301 Study Group, *et al*. The efficacy and safety of tigecycline for the treatment of complicated intra-abdominal infections: Analysis of pooled clinical trial data. Clin Infect Dis 2005;41 Suppl 5:S354-67.
32. Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJ, *et al*. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis 2005;41:1373-406.
33. Andersson D. The Ways in Which Bacteria Resist Antibiotics. Geneva: World Health Organization; 2005.
34. Tuckman M, Petersen PJ, Howe AY, Orlowski M, Mullen S, Chan K, *et al*. Occurrence of tetracycline resistance genes among *Escherichia coli* isolates from the phase 3 clinical trials for tigecycline. Antimicrob Agents Chemother 2007;51:3205-11.
35. Chopra I. Glycylcyclines: Third-generation tetracycline antibiotics. Curr Opin Pharmacol 2001;1:464-9.
36. Chopra I, Roberts M. Tetracycline antibiotics: Mode of action, applications, molecular biology, and epidemiology of bacterial resistance. Microbiol Mol Biol Rev 2001;65:232-60.
37. Livermore DM. Tigecycline: What is it, and where should it be used? J Antimicrob Chemother 2005;56:611-4.
38. Khardori N. Antibiotics--past, present, and future. Med Clin North Am 2006;90:1049-76.
39. Dean CR, Visalli MA, Projan SJ, Sum PE, Bradford PA. Efflux-mediated resistance to tigecycline (GAR-936) in *Pseudomonas aeruginosa* PAO1. Antimicrob Agents Chemother 2003;47:972-8.
40. Visalli MA, Murphy E, Projan SJ, Bradford PA. AcrAB multidrug efflux pump is associated with reduced levels of susceptibility to tigecycline (GAR-936) in *Proteus mirabilis*. Antimicrob Agents Chemother 2003;47:665-9.
41. Hirata T, Saito A, Nishino K, Tamura N, Yamaguchi A. Effects of efflux transporter genes on susceptibility of *Escherichia coli* to tigecycline (GAR-936). Antimicrob Agents Chemother 2004;48:2179-84.
42. Ruzin A, Visalli MA, Keeney D, Bradford PA. Influence of transcriptional activator RamA on expression of multidrug efflux pump AcrAB and tigecycline susceptibility in *Klebsiella pneumoniae*. Antimicrob Agents Chemother 2005;49:1017-22.
43. Moore IF, Hughes DW, Wright GD. Tigecycline is modified by the flavin-dependent monooxygenase TetX. Biochemistry 2005;44:11829-35.
44. McAleese F, Petersen P, Ruzin A, Dunman PM, Murphy E, Projan SJ, *et al*. A novel MATE family efflux pump contributes to the reduced susceptibility of laboratory-derived *Staphylococcus aureus* mutants to tigecycline. Antimicrob Agents Chemother 2005;49:1865-71.
45. Keeney D, Ruzin A, Bradford PA. RamA, a transcriptional regulator, and AcrAB, an RND-type efflux pump, are associated with decreased susceptibility to tigecycline in *Enterobacter cloacae*. Microb Drug Resist 2007;13:1-6.
46. Peleg AY, Adams J, Paterson DL. Tigecycline efflux as a mechanism for nonsusceptibility in *Acinetobacter baumannii*. Antimicrob Agents Chemother 2007;51:2065-9.
47. Keeney D, Ruzin A, McAleese F, Murphy E, Bradford PA. MarA-mediated overexpression of the AcrAB efflux pump results in

decreased susceptibility to tigecycline in *Escherichia coli*. J Antimicrob Chemother 2008;61:46-53.
48. Bratu S, Landman D, George A, Salvani J, Quale J. Correlation of the expression of acrB and the regulatory genes *marA*, *soxS* and *ramA* with antimicrobial resistance in clinical isolates of *Klebsiella pneumoniae* endemic to New York City. J Antimicrob Chemother 2009;64:278-83.
49. Rajendran R, Quinn RF, Murray C, McCulloch E, Williams C, Ramage G. Efflux pumps may play a role in tigecycline resistance in *Burkholderia* species. Int J Antimicrob Agents 2010;36:151-4.
50. Hentschke M, Christner M, Sobottka I, Aepfelbacher M, Rohde H. Combined ramR mutation and presence of a Tn1721-associated tet(A) variant in a clinical isolate of *Salmonella enterica* serovar Hadar resistant to tigecycline. Antimicrob Agents Chemother 2010;54:1319-22.
51. Hornsey M, Ellington MJ, Doumith M, Scott G, Livermore DM, Woodford N. Emergence of AcrAB-mediated tigecycline resistance in a clinical isolate of *Enterobacter cloacae* during ciprofloxacin treatment. Int J Antimicrob Agents 2010;35:478-81.
52. Hentschke M, Wolters M, Sobottka I, Rohde H, Aepfelbacher M. ramR mutations in clinical isolates of *Klebsiella pneumoniae* with reduced susceptibility to tigecycline. Antimicrob Agents Chemother 2010;54:2720-3.
53. Sun JR, Chan MC, Chang TY, Wang WY, Chiueh TS. Overexpression of the adeB gene in clinical isolates of tigecycline-nonsusceptible *Acinetobacter baumannii* without insertion mutations in adeRS. Antimicrob Agents Chemother 2010;54:4934-8.
54. Ruzin A, Immermann FW, Bradford PA. RT-PCR and statistical analyses of adeABC expression in clinical isolates of *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex. Microb Drug Resist 2010;16:87-9.
55. Hornsey M, Ellington MJ, Doumith M, Hudson S, Livermore DM, Woodford N. Tigecycline resistance in *Serratia marcescens* associated with up-regulation of the SdeXY-HasF efflux system also active against ciprofloxacin and cefpirome. J Antimicrob Chemother 2010;65:479-82.
56. Horiyama T, Nikaido E, Yamaguchi A, Nishino K. Roles of *Salmonella* multidrug efflux pumps in tigecycline resistance. J Antimicrob Chemother 2011;66:105-10.
57. Rosenblum R, Khan E, Gonzalez G, Hasan R, Schneiders T. Genetic regulation of the ramA locus and its expression in clinical isolates of *Klebsiella pneumoniae*. Int J Antimicrob Agents 2011;38:39-45.
58. Bartha NA, Sóki J, Urbán E, Nagy E. Investigation of the prevalence of tetQ, tetX and tetX1 genes in *Bacteroides* strains with elevated tigecycline minimum inhibitory concentrations. Int J Antimicrob Agents 2011;38:522-5.
59. Volkers G, Palm GJ, Weiss MS, Wright GD, Hinrichs W. Structural basis for a new tetracycline resistance mechanism relying on the TetX monooxygenase. FEBS Lett 2011;585:1061-6.
60. Huemer M, Mairpady Shambat S, Brugger SD, Zinkernagel AS. Antibiotic resistance and persistence-Implications for human health and treatment perspectives. EMBO Rep 2020;21:e51034.
61. Duffey M, Jumde RP, Da Costa RM, Ropponen HK, Blasco B, Piddock LJ. Extending the potency and lifespan of antibiotics: Inhibitors of gram-negative bacterial efflux pumps. ACS Infect Dis 2024;10:1458-82.
62. He F, Fu Y, Chen Q, Ruan Z, Hua X, Zhou H, *et al*. Tigecycline susceptibility and the role of efflux pumps in tigecycline resistance in KPC-producing *Klebsiella pneumoniae*. PLoS One 2015;10:e0119064.
63. Li F, Xu T, Fang D, Wang Z, Liu Y. Restoring tigecycline efficacy with lysine supplementation in tmexCD-toprJ-positive bacteria. Int J Antimicrob Agents 2025;66:107511.
64. Sun L, Sun L, Li X, Hu X, Wang X, Nie T, *et al*. A novel tigecycline adjuvant ML-7 reverses the susceptibility of tigecycline-resistant *Klebsiella pneumoniae*. Front Cell Infect Microbiol 2021;11:809542.
65. Medindia. Tigecycline Drug Price and Information; 2023. Available from: https://www.medindia.net/drug-price/tigecycline.htm [Last accessed on 2026 Jul].
66. Zimmerman JJ, Harper DM, Matschke K, Speth JL, Raible DG, Fruncillo RJ. Absence of an interaction between tigecycline and digoxin in healthy men. Pharmacotherapy 2007;27:835-44.
67. Pfizer Limited. Tygacil 50 mg Powder for Solution for Infusion. Electronic Medicines Compendium; 2015. Available from: https://www.medicines.org.uk/emc/medicine/17779 [Last accessed on 2025 Dec].
68. Sovrlić M, Mrkalić E, Jelić R, Serafinović MC, Stojanović S, Prodanović N, *et al*. Effect of caffeine and flavonoids on the binding of tigecycline to human serum albumin: A spectroscopic study and molecular docking. Pharmaceuticals (Basel) 2022;15:266.
69. Dou M. Clinical analysis and rational evaluation of 25 cases of tigecycline: A cross-sectional study. Medicine (Baltimore) 2025;104:e45522.