For the use only of a Registered Medical Practitioner of a Hospital or a Laboratory

℞ Tigecycline For Injection IP

Lyophilized Cake Form

AMERICAN
TIGICAN 50
Injection

50 mg/Vial

For I.V Infusion use only

Composition :

Each vial contains :

Tigecycline (Sterile) (Lyophilized)	IP	50 mg
Excipient		q.s.

Dose Form: Powder for solution for injection

Description

(Tigecycline) is a tetracycline derivative (a glycylcycline) for intravenous infusion.

Pharmacodynamic properties :

Tigecycline *is* bacteriostatic *and* is a protein synthesis inhibitor by binding to the 30S ribosomal subunit of bacteria and thereby blocking entry of Aminoacyl-tRNA into the A site of the ribosome during prokaryotic translation.

Mechanism of action

Tigecycline, a glycylcycline antibiotic, inhibits protein translation in bacteria by binding to the 30S ribosomal subunit and blocking entry of amino-acyl tRNA molecules into the A site of the ribosome. This prevents incorporation of amino acid residues into elongating peptide chains.

In general, tigecycline is considered bacteriostatic. At 4 times the minimum inhibitory concentration (MIC), a 2-log reduction in colony counts was observed with tigecycline against *Enterococcus* spp., *Staphylococcus aureus*, and *Escherichia coli*.

Mechanism of resistance

Tigecycline is able to overcome the two major tetracycline resistance mechanisms, ribosomal protection and efflux. Cross-resistance between tigecycline and minocycline-resistant isolates among the *Enterobacteriaceae* due to multi-drug resistance (MDR) efflux pumps has been shown. There is no target-based cross-resistance between tigecycline and most classes of antibiotics.

Pharmacokinetic properties

Absorption Tigecycline is administered intravenously and therefore has 100 % bioavailability.

Distribution

The in vitro plasma protein binding of tigecycline ranges from approximately 71 % to 89 % at concentrations observed in clinical studies (0.1 to 1.0 mcg/ml). Human pharmacokinetic studies have demonstrated that tigecycline readily distributes to tissues.

In humans, the steady-state volume of distribution of tigecycline averaged 500 to 700 L (7 to 9 L/kg), indicating that tigecycline is extensively distributed beyond the plasma volume and concentrates into tissues. No data are available on whether tigecycline can cross the blood-brain barrier in humans.

In clinical pharmacology studies using the therapeutic dosage regimen of 100 mg followed by 50 mg q12h, serum tigecycline steady-state C_{max} was 866±233 ng/ml for 30-minute infusions and 634±97 ng/ml for 60-minute infusions. The steady-state $AUC_{0\text{-}12h}$ was 2349±850 ngh/ml.

Biotransformation

On average, it is estimated that less than 20 % of tigecycline is metabolised before excretion. In healthy male volunteers, following the administration of ^{14}C-tigecycline, unchanged tigecycline was the primary ^{14}C-labelled material recovered in urine and faeces, but a glucuronide, an N-acetyl metabolite and a tigecyclineepimer were also present.

In vitro studies in human liver microsomes indicate that tigecycline does not inhibit metabolism mediated by any of the following 6 cytochrome P450 (CYP) isoforms: 1A2, 2C8, 2C9, 2C19, 2D6, and 3A4 by competitive inhibition. In addition, tigecycline did not show NADPH-dependency in the inhibition of CYP2C9, CYP2C19, CYP2D6 and CYP3A, suggesting the absence of mechanism-based inhibition of these CYP enzymes.

Elimination

The recovery of total radioactivity in feces and urine following administration of ^{14}C-tigecycline indicates that 59% of the dose is eliminated by biliary/fecal excretion, and 33% is excreted in urine. Approximately 22% of the total dose is excreted as unchanged tigecycline in urine. Overall, the primary route of elimination for tigecycline is biliary excretion of unchanged tigecycline and its metabolites. Glucuronidation and renal excretion of unchanged tigecycline are secondary routes.

Indications

Tigecycline is given intravenously and has activity against a variety of Gram-positive and Gram-negative bacterial pathogens, many of which are resistant to existing antibiotics. Tigecycline successfully to treat complicated skin and skin structure infections (cSSSI),.[5]Tigecycline is active against many Gram-positive bacteria, Gram-negative bacteria and anaerobes – including activity against methicillin-resistant Staphylococcus aureus (MRSA), Stenotrophomonasmaltophilia, Haemophilusinfluenzae, and Neisseria gonorrhoeae (with MIC values reported at 2 μg/mL) and multi-drug resistant strains of Acinetobacterbaumannii. It has no activity against Pseudomonas spp. or Proteus spp. The drug is licenced for the treatment of skin and soft tissue infections as well as intra-abdominal infections.

Susceptibility data

Tigecycline targets both Gram positive and Gram negative bacteria including a few key multi-drug resistant pathogens. The following represents MIC susceptibility data for a few medically significant bacterial pathogens.

Escherichia coli: 0.015 mg/ml - 4 mg/ml
Klebsiellapneumoniae: 0.06 mg/ml - 16 mg/ml
Staphylococcus aureus (methicillin-resistant): 0.03 mg/ml - 2 mg/ml

Reconstitution and Method of Administration

Each vial of tigecycline should be reconstituted with 5.0 ml of 0.9 % Sodium Chloride IP, or Dextrose IP, to achieve a concentration of 10 mg,ml of tigecycline.

The vial should be gently swirled until the drug dissolves. Immediately withdraw 5 ml of the reconstituted solution from the vial and add to a 100 ml IV bag for infusion (for a 100 mg dose, reconstituted two vials for a 50 mg dose, reconstituted one vial) The maximum concentration in the IV bag should be 1mg/ml. the reconstituted solution should be yelow to orange in colour, if not the solution should be discarded. parenteral drug products should be inspected visually (or particulate matter and discoloration (e.g., green or black) prior to administration.

Stability and Compatibility :

Prior to reconstitution tigecycline should be store below 30° C reconstituted solution must be immediately transferred and further diluted for IV infusion.

Reconstituted solution may be stored in the IV bag at room temperature for upto 6 hours, or refrigerated at 2-8° C or upto 24 hours.

Dosing

Tigecycline is given by slow intravenous infusion (30 to 60 minutes). A single dose of 100 mg is given first,

followed by 50 mg every twelve hours after that. Patients with impaired liver function need to be given a lower dose. No adjustment is needed for patients with impaired kidney function. It is not licensed for use in children. There is no oral form available.

Side effects

Tigecycline has similar side effects to the tetracyclines. The most common side effects of tigecycline are diarrhea, nausea and vomiting. Nausea and vomiting is mild or moderate and usually occurs during the first two days of therapy. Other side effects include pain at the injection site, swelling and irritation; increased or decreased heart rate and infections. Also avoid use in children and pregnancy, due to its effects on teeth and bone. As with other antibiotics, overgrowth of organisms that are not susceptible to tigecycline can occur.Tigecycline showed an *Increased* mortality in patients treated for hospital-acquired pneumonia, especially ventilator-associated pneumonia (a non-approved use), but also in patients with complicated skin and skin structure infections, complicated intra-abdominal infections and diabetic foot infection. Increased mortality was in comparison to other treatment of the same types of infections. The difference was not statistically significant for any type, but mortality was numerically greater for every infection type with Tigecycline treatment, and prompted a black box warning

Precaution & Warning

Tigecycline may cause serious allergic reactions, including anaphylaxis, which can be life-threatening and require immediate medical attention. if you have itching, hives, hoarseness, trouble breathing, trouble swallowing, or any swelling of your hands, face, or mouth after you receive this medicine.

Use In Specific Populations

Pregnancy

There are no adequate and well-controlled studies of tigecycline in pregnant women. Tigecycline should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Tigecycline is administered to a nursing woman.

Pediatric Use

Use in patients under 18 years of age is not recommended. Safety and effectiveness in pediatric patients below the age of 18 years have not been established. Because of the increased mortality observed in tigecycline-treated adult patients in clinical trials, pediatric trials of tigecycline to evaluate the safety and efficacy of tigecycline were not conducted. In situations where there are no other alternative antibacterial drugs, pediatric dosing has been proposed based on data from pediatric pharmacokinetic studies Because of effects on tooth development, use in patients under 8 years of age is not recommended.

Geriatric Use

No significant difference in tigecycline exposure was observed between healthy elderly subjects and younger subjects following a single 100 mg dose of tigecycline.

Contraindications

Patients hypersensitive to tetracycline class antibiotics may be hypersensitive to tigecycline.

Storage : Store protected from light and moisture, at a temperature not exceeding 30°C. Improper storage may be deteriorate the product.

Overdose

No specific information is available on the treatment of overdosage. Intravenous administration of tigecycline at a single dose of 300 mg over 60 minutes in healthy volunteers resulted in an increased incidence of nausea and vomiting. Tigecycline is not removed in significant quantities by haemodialysis.

Shelf Life 24 Months

Presentation : Tigecycline For Injection IP 50 mg/vial

Tigecycline For Injection IP is a yellow colour powder filled in vial.

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