THE NORTHERN HOSPITAL

TIGECYCLINE

Introduction

Tigecycline is the first clinically available **glycylcycline** antibiotic, derived from the tetracycline antibiotic minocycline.

It is a board spectrum bacteriostatic antibiotic that has activity against many of the emerging *multiresistant* bacterial organisms, including CRE.

History

Tigecycline was given fast-track approval by the U.S. Food and Drug Administration (FDA) on June 17, 2005, in order to treat serious infections from emerging multiresistant bacteria.

Chemistry

Tigecycline is a **glycylcycline** antibiotic.

It is the first clinically available drug in a new class of antibiotics called the **glycylcyclines.**

It is structurally similar to the **tetracyclines** in that it contains a central four-ring carbocyclic skeleton and is actually a derivative of minocycline.

Tigecycline has a substitution at the D-9 position which is believed to confer broad spectrum activity.

Classification

Tigecycline is a **glycylcycline** antibiotic.

Preparation

Ampoules:

- **50 mg (as powder for reconstitution)/ 5 ml ampoule**

  Note that the reconstituted solution is **yellow to orange.**

Mechanism of Action

Tigecycline is a bacteriostatic antibiotic that binds to the 30S ribosomal subunit of bacteria thus preventing bacterial protein synthesis.

Tigecycline is not affected by beta-lactamase (including extended spectrum beta-lactamase) resistance mechanisms.

Tigecycline is not affected by the major tetracycline resistance mechanism of ribosomal protection

Pharmacokinetics

Absorption:

- Tigecycline is given **intravenously.**

Distribution:

- Tigecycline is well distributed to most tissues.

Metabolism and excretion:

- Tigecycline is *not* extensively metabolised.
- It is predominantly excreted in the bile and in the urine.

Pharmacodynamics

Tigecycline is a broad-spectrum antibiotic, with activity against many multiresistant bacteria, including: [1]

1. Gram-positive bacteria:
    - Including methicillin-resistant *Staphylococcus aureus* (MRSA).
2. Gram-negative aerobic bacteria:

    Including:

    - Vancomycin-resistant enterococci (VRE)
    - Some CRE organisms (but not *Pseudomonas aeruginosa*)
3. Anaerobic bacteria
4. Rapidly growing non-tuberculous mycobacteria.

However, data show that outcomes are worse with tigecycline compared with other first antimicrobials, so it is not recommended as first-line treatment for severe infection, unless this is caused by a multiresistant organism.

Note that, as for all antibiotics, the prevalence of bacterial resistance may vary geographically and over time for selected species and local information on resistance is also important, particularly when treating severe infections.

Indications

These include:

- Complicated intra-abdominal infections due to susceptible organisms, where other treatment is unsuitable

- Complicated skin and soft tissue infections due to susceptible organisms, where other treatment is unsuitable

Contraindications/ Precautions

These include:

1. Known allergy to tigecycline or other tetracyclines.

2. **Tetracyclines in general are contraindicated in children < 8 years:**

    - The principle period of risk is during tooth development which occurs in the latter half of pregnancy, infancy and childhood to the age of 8 years)

    - Note however that because dentine development continues in some children after this age, some practitioners avoid the use of tetracyclines in children up to the age of **12 years**. [1]

3. Severe hepatic impairment**:**

    - Reduce the dose in patients with severe impairment and monitor response carefully.

    - About half a tigecycline dose is excreted in the bile; how this is affected by cholestasis however is unknown.

Pregnancy

As tigecycline is derived from the tetracycline, minocycline, it is classified as a class D drug with respect to pregnancy.

Class D drugs are those drugs which have caused, are suspected to have caused or may be expected to cause an increased incidence of human fetal malformations or irreversible

damage. These drugs may also have adverse pharmacological effects. Specialised texts should be consulted for further details.

Breast feeding

Not recommended in breast feeding women.

Adverse Effects

Tigecycline may have similar adverse effects to the tetracyclines as it is derived from minocycline.

These may therefore include:

1. Known hypersensitivity to any of the tetracyclines - use cautiously.

2. GIT upset, (as with most antibiotics).

3. Tetracyclines given to children can:

    - Discolour teeth
    - Cause enamel dysplasia, which increases the risk of dental caries.
    - Be deposited in bone, causing deformities and inhibiting bone growth.

4. Dermatological:

    - Photosensitivity rashes
    - Occasionally severe reactions such as Stevens-Johnson syndrome.

5. Pseudomembranous colitis:

    - Pseudomembranous colitis has been reported with nearly all antibacterial agents, including tetracyclines, and may range in severity from mild to life-threatening.

      Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

Dosing

Usual adult dosing is:

- **IV 100 mg IV for the first dose, then 50 mg every 12 hours.**

Dilute to 100 mL in sodium chloride 0.9% or glucose 5% and infuse slowly over 30 - 60 minutes.

References

1. eTG - March 2015.

    - Antibiotic Therapeutic Guidelines 15th ed 2014.

2. Tigecycline in Australian Medicines Handbook, Accessed June 2015.

3. Tigecycline in MIMs 1 January 2014.

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June 2015.